Dissertation On

TO STUDY THE ROLE OF fT3AND rT3 IN PREDICTING THE MORTALITYAND MORBIDITY IN STEMI AND NSTEMI PATIENTS.

Submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI- 600 032

In partial fulfilment of regulations
For the award of the degree

M.D (GENERAL MEDICINE)

BRANCH – I

ESIC - MEDICAL COLLEGE& POSTGRADUATE INSTITUTE OF MEDICAL SCIENCE AND RESEARCH,

K.K.NAGAR, CHENNAI –78.

APRIL 2017

ENDORSEMENT BY THE DEAN/

THE HEAD OF THE INSTITUTION

This is to certify that this dissertation titled **" TO STUDY THE ROLE OF fT3 AND rT3 IN PREDICTING THE MORTALITY & MORBIDITY IN STEMI AND NSTEMI PATIENTS"** submitted by **Dr.G.Sakthiram**, appearing for M.D Degree Branch – 1, GENERAL MEDICINE examination in April 2017 is a bonafide research work done by him in partial fulfilment of the regulations of The Tamilnadu Dr. M.G.R Medical University, Chennai. I forward this to the Tamilnadu Dr. M.G.R Medical University, Chennai,Tamilnadu, India.

DEAN

Dr. SRIKUMARI DAMODARAM,

M.S.,M.Ch.(SGE), M.A.M.S., F.A.C.S.,

F.I.C.S.,F.M.M.C

ESIC MEDICAL COLLEGE & PGIMSR

K.K.NAGAR, CHENNAI-78.

Date:

Place: Chennai

CERTIFICATE BY THE HEAD OF DEPARTMENT

This is to certify that this dissertation titled "**TO STUDY THE ROLE OF fT3 AND rT3 IN PREDICTING THE MORTALITY & MORBIDITY IN STEMI AND NSTEMI PATIENTS**" is a bonafide research work done by **Dr.G.Sakthiram**, in partial fulfilment of the regulations for the degree of M.D. in General Medicine.

PROF. DR. A.R.MALATHY. MD.,

Professor and Head,

Department of General medicine,

ESIC Medical College & PGIMSR,

Chennai -78.

Date:

Place: Chennai

CERTIFICATE OF GUIDE

This is to certify that this dissertation named "**TO STUDY THE ROLE OF fT3 AND rT3 IN PREDICTING THE MORTALITY AND MORBIDITY IN STEMI AND NSTEMI PATIENTS**" is a bonafide work performed by **Dr.G.Sakthiram**, post graduate student, Department of General medicine, ESIC Medical College & PGIMSR, Chennai-78, under my guidance and supervision in partial fulfilment of regulations of The Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree during the academic year 2014-2017.

PROF. DR. A.R.MALATHY. MD.,

Professor and Head,

Department of General medicine,

ESIC Medical College & PGIMSR,

Chennai -78

Date:

Place: Chennai

DECLARATION

I solemnly declare that this dissertation entitled "**TO STUDY THE ROLE OF fT3 AND rT3 IN PREDICTING THE MORTALITY AND MORBIDITY IN STEMI AND NSTEMI PATIENTS**" has been conducted by me at ESIC Medical College & PGIMSR, Chennai, under the guidance and supervision of **Prof.Dr.A.R.Malathy, M.D**., Professor and Head, Department of General Medicine, ESIC Medical College & PGIMSR, Chennai-78. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the University regulations for the award of the degree of M.D. Branch 1 (General Medicine).

SIGNATURE OF THE CANDIDATE
Dr. G.SAKTHIRAM
M.D. Post Graduate
Dept. Of General Medicine
ESIC Medical College & PGIMSR
KK Nagar, Chennai-78

Date:

Place: Chennai

DECLARATION BY THE CANDIDATE

I hereby declare that The Tamilnadu Dr. M.G.R. Medical University, Chennai, shall have the rights to preserve, use and disseminate this dissertation/thesis in print/electronic format for academic/ research purpose.

SIGNATURE OF THE CANDIDATE

DR. G.SAKTHIRAM

Place:

Date:

ACKNOWLEDGEMENT

It is my immense pleasure to thank everyone who contributed in compilation of this study.

At the outset, I would like to thank our respected Dean, **Prof.Dr.Srikumari Damodaram., M.S., M.Ch (SGE)., M.A.M.S., F.A.C.S., F.I.C.S., F.M.M.C**., for her kind permission to conduct the study.

I am greatly indebted to **Prof.Dr.A.R.Malathy, M.D**., Professor and Head, Department of General Medicine, ESIC Medical College & PGIMSR, who was my guide for the dissertation. I thank her wholeheartedly for her able guidance and encouragement throughout the study.

I am thankful to **Prof. Jemima Bhaskar. M.D**., former Associate Professor, Department of General Medicine,, ESIC Medical College & PGIMSR for her guidance in the study.

I express my sincere thanks to all the doctors of the Department of General Medicine, ESIC Medical College & PGIMSR**, Dr.Kannan, Dr.Nalini, Dr.Suganya, Dr.Nandagopal, Dr.Sebasan, Dr.Jagadeesan, Dr.Hari Prasad, Dr.Samuthiravel, Dr.Poornima Raj, Dr.Karthika,**

and **Dr. Chitradevi** for their strong support and encouragement throughout this study.

I thank **Dr.Porchelvan**, statistician, Department of community medicine at Saveetha Medical College for his help in the statistical analysis of the study.

I also extend my sincere thanks to the Department of Biochemistry and Department of cardiology for their valuable support throughout the study.

I will always remember with an extreme sense of thankfulness, the cooperation and criticism shown by my fellow post graduate colleagues & friends.

I would like to extend my gratitude to my beloved family members for their unconditional support in completing my work.

Finally, I wholeheartedly thank the patients, who were the subjects of the study, without whom this would not have become a reality.

DR. G.SAKTHIRAM

CERTIFICATE OF APPROVAL

To

Dr. G. Sakthiram,
PG in Department of General Medicine,
ESIC Medical College & PGIMSR,
KK Nagar, Chennai-78.

Dear Dr. G.Sakthiram,

The Institutional Ethical Committee of ESIC Medical College & PGIMSR reviewed and discussed your application for approval of the proposal entitled **"To study the role of fT3 and rT3 in predicting the mortality and morbidity in STEMI and NSTEMI patients"** at ESIC Medical College & PGIMSR, K.K.Nagar, Chennai 600 078", **No. 02/27/10/2014**..

The following members of the Ethical Committee were present in the meeting held on 27.10.2014 conducted at ESIC Medical College & PGIMSR, KK Nagar, Chennai-78.

S.No.	ETHICAL COMMITTEE MEMBERS
1.	Prof. A.V. Srinivasan, Chairperson, EC Member EMERITUS Professor, The Tamilnadu Dr. MGR Medical University Former Prof. & HOD., of Institute of Neurology, Madras Medical College
2.	Prof.V.Rajalakshmi, Vice Principal, ESIC Medical College & PGIMSR, EC Member
3.	Prof.M.Kanaheswari, Medical Superintendent, ESIC Medical College & PGIMSR, EC Member
4.	Prof. Kamalini Sridharan, Registrar, ESIC Medical College & PGIMSR, EC Member
5.	Prof. S. Seethalakshmi, Prof. & HOD, Department of Pharmacology, ESIC Medical College & PGIMSR, EC Member
6.	Prof. S. Malliga, Prof. & HOD, Department of Biochemistry, ESIC Medical College & PGIMSR, EC Member
7.	Prof. Sowmya Sampath, Prof. & HOD, Department of Paediatrics, ESIC Medical College & PGIMSR, EC Member
8.	Prof. Usha Kothandaraman, Prof. & HOD, Department of Anatomy, ESIC Medical College & PGIMSR, EC Member
9.	Dr. Aruna Patil Bholenath, Assistant Professor, Department of Community Medicine, ESIC Medical College & PGIMSR, EC Member
10.	Dr. A. Sundaram, Dept. of Medicine [Diabetologist], EC Member
11.	Dr. O.L. Naganath Babu, Dept. of Surgical Gastroenterology, EC Member
12.	Dr. S. Dhanalakshmi, Dept. of OBG, EC Member
13.	Dr. Rajkumar Williams, Dept. of Surgery, EC Member
14.	Prof. C. Rajendiran, Department of General Medicine, EC Member
15	Dr. C.V. Aravindan, Scientist, EC Member
16.	Shri. K M Venugopal, Advocate, EC Member

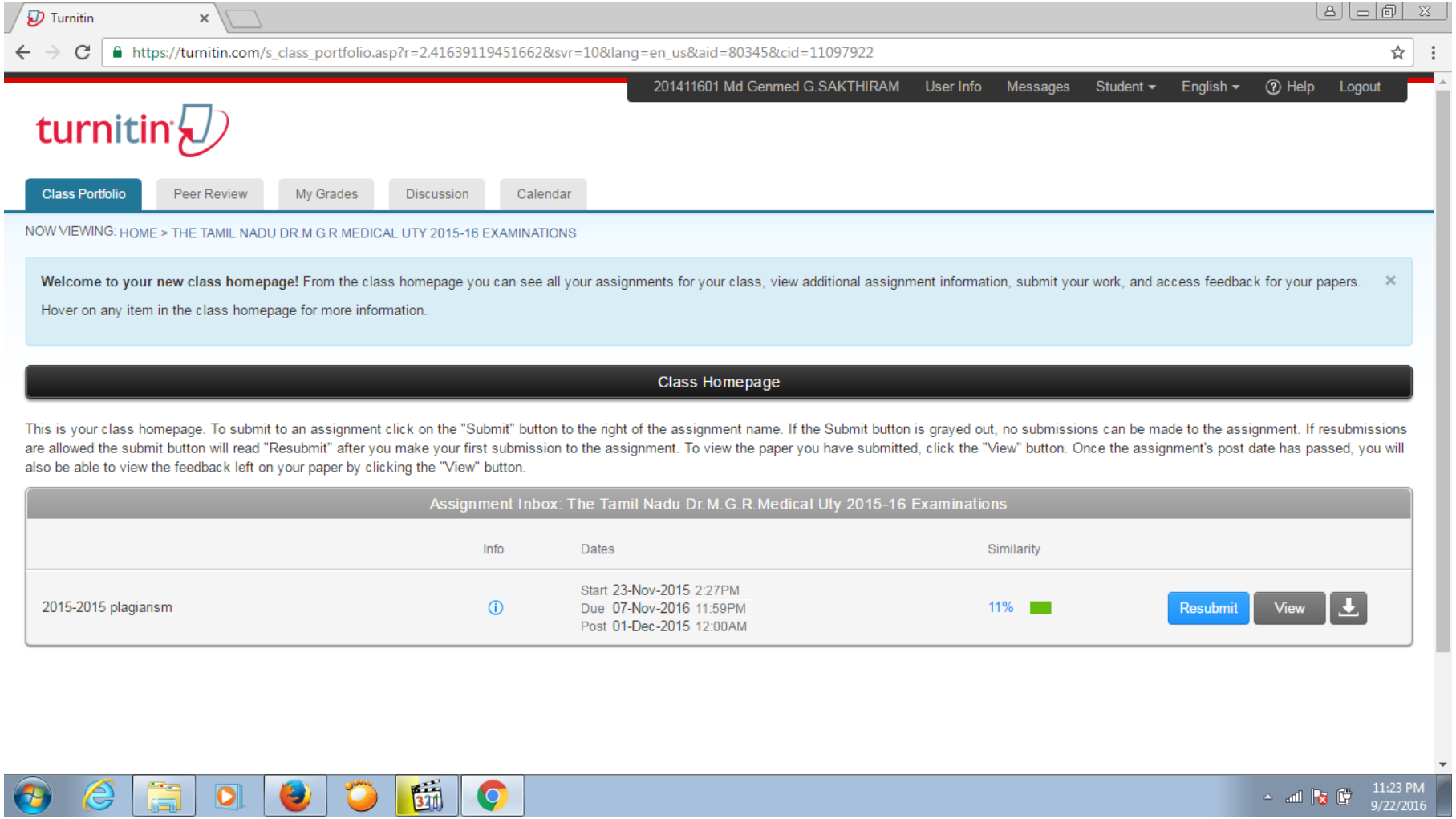
The proposal is approved to be conducted in its presented form.

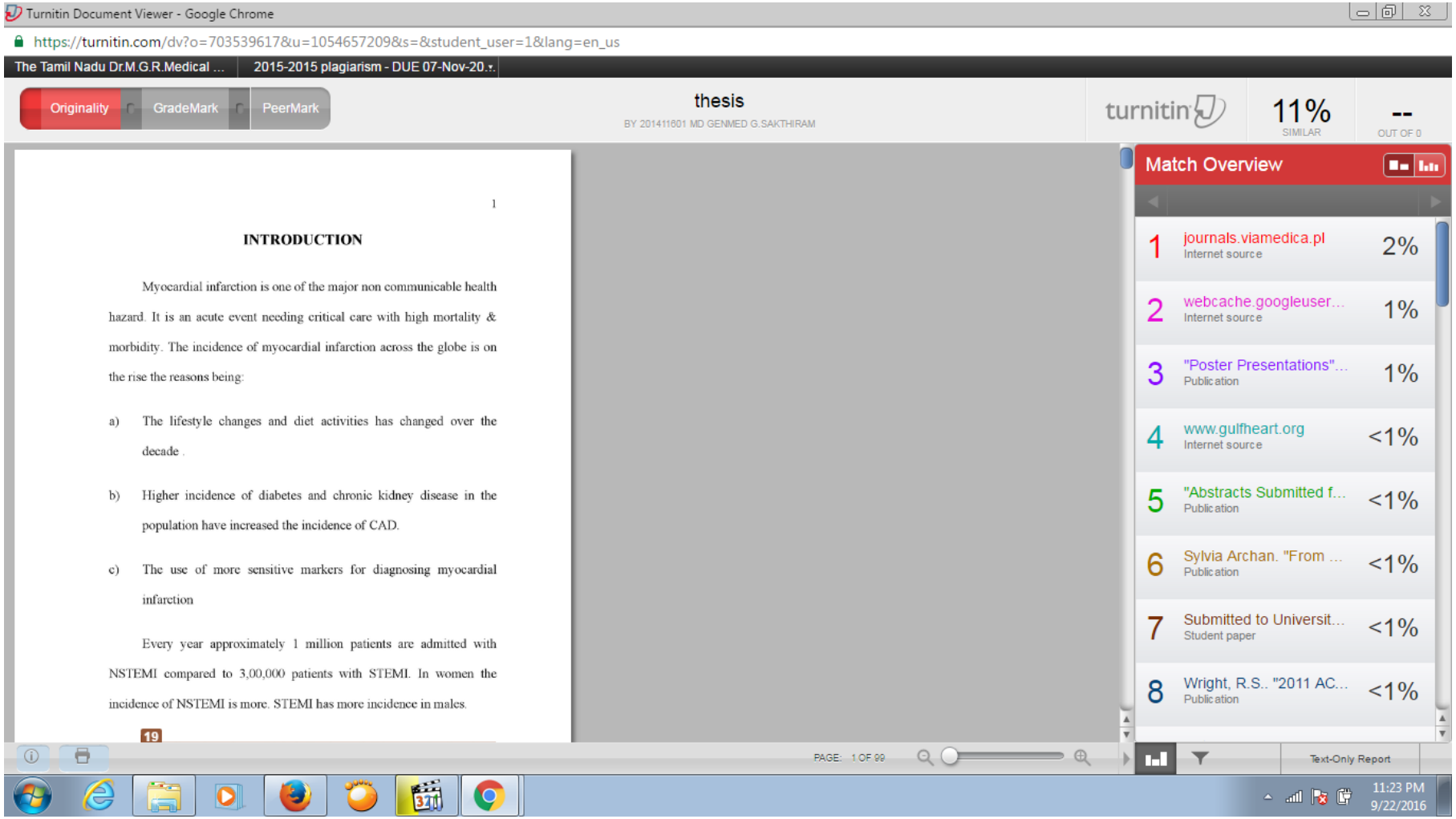
The Institutional Ethical Committee expects to be informed about the progress of the study and significant adverse effects occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Date : 27.10.2014
Place : Chennai-78

[DR.A.V.SRINIVASAN]
CHAIRPERSON
ETHICAL COMMITTEE

PLAGIARISM


Turnitin
https://turnitin.com/s_class_portfolio.asp?r=2.41639119451662&svr=10&lang=en_us&aid=80345&cid=11097922
201411601 Md Genmed G.SAKTHIRAM
User Info
Messages
Student
English
Help
Logout
turnitin
Class Portfolio
Peer Review
My Grades
Discussion
Calendar
NOW VIEWING: HOME > THE TAMIL NADU DR.M.G.R.MEDICAL UTY 2015-16 EXAMINATIONS
Welcome to your new class homepage! From the class homepage you can see all your assignments for your class, view additional assignment information, submit your work, and access feedback for your papers.
Hover on any item in the class homepage for more information.
Class Homepage
This is your class homepage. To submit to an assignment click on the "Submit" button to the right of the assignment name. If the Submit button is grayed out, no submissions can be made to the assignment. If resubmissions are allowed the submit button will read "Resubmit" after you make your first submission to the assignment. To view the paper you have submitted, click the "View" button. Once the assignment's post date has passed, you will also be able to view the feedback left on your paper by clicking the "View" button.
Assignment Inbox: The Tamil Nadu Dr.M.G.R.Medical Uty 2015-16 Examinations
Info
Dates
Similarity
2015-2015 plagiarism
Start 23-Nov-2015 2:27PM
Due 07-Nov-2016 11:59PM
Post 01-Dec-2015 12:00AM
11%
Resubmit
View
11:23 PM
9/22/2016


Turnitin Document Viewer - Google Chrome
https://turnitin.com/dv?o=703539617&u=1054657209&s=&student_user=1&lang=en_us
The Tamil Nadu Dr.M.G.R.Medical ...
2015-2015 plagiarism - DUE 07-Nov-20...
Originality
GradeMark
PeerMark
thesis
BY 201411601 MD GENMED G.SAKTHIRAM
turnitin
11%
SIMILAR
--
OUT OF 0
1
INTRODUCTION
Myocardial infarction is one of the major non communicable health hazard. It is an acute event needing critical care with high mortality & morbidity. The incidence of myocardial infarction across the globe is on the rise the reasons being:
a) The lifestyle changes and diet activities has changed over the decade .
b) Higher incidence of diabetes and chronic kidney disease in the population have increased the incidence of CAD.
c) The use of more sensitive markers for diagnosing myocardial infarction
Every year approximately 1 million patients are admitted with NSTEMI compared to 3,00,000 patients with STEMI. In women the incidence of NSTEMI is more. STEMI has more incidence in males.
19
PAGE: 1 OF 99
Match Overview
1 journals.viamedica.pl Internet source 2%
2 webcache.googleuser... Internet source 1%
3 "Poster Presentations"... Publication 1%
4 www.gulfheart.org Internet source <1%
5 "Abstracts Submitted f... Publication <1%
6 Sylvia Archan. "From ... Publication <1%
7 Submitted to Universit... Student paper <1%
8 Wright, R.S.. "2011 AC... Publication <1%
Text-Only Report
11:23 PM
9/22/2016

LIST OF ABBREVIATIONS

1.	**ECG**	**–**	**Electrocardiogram**
2.	**STEMI**	**–**	**ST elevation myocardial infarction**
3.	**NSTEMI**	**–**	**Non ST elevation myocardial infarction.**
4.	**LBBB**	**–**	**Left bundle branch block.**
5.	**PCI**	**–**	**Percutaneous coronary intervention.**
6.	**CABG**	**–**	**Coronary artery bypass grafting.**
7.	**GP**	**–**	**Glycoprotein.**
8.	**ADP**	**–**	**Adenosine di phosphate.**
9.	**MI**	**–**	**Myocardial infarction.**
10.	**FMC**	**–**	**First medical contact.**
11.	**AV**	**–**	**Arteriovenous.**
12.	**CPR**	**–**	**Cardiopulmonary resuscitation.**
13.	**CAG**	**–**	**Coronary angiogram.**
14.	**LMWH**	**–**	**Low molecular weight heparin.**
15.	**HIT**	**–**	**Heparin induced thrombocytopenia.**
16.	**aPtt**	**–**	**Activated partial thromboplastin time.**
17.	**JVP**	**–**	**Jugular venous pulse.**
18.	**RV**	**–**	**Right ventricle.**
19.	**MIT**	**–**	**Mono iodotyrosinase.**

20.	**DIT**	**–**	**Di iodotyrosinase.**
21.	**RXR**	**–**	**Retinod-x-receptor.**
22.	**EF**	**–**	**Ejection fraction.**
23.	**ICU**	**–**	**Intensive care unit.**
24.	**AWMI**	**–**	**Anterior wall myocardial infarction.**
25.	**IPWMI**	**–**	**Inferoposterior wall myocardial infarction.**
26.	**LWMI**	**–**	**Lateral wall myocardial infarction.**
27.	**COPD**	**-**	**Chronic obstructive pulmonary disease**
28.	**HSCRP**	**-**	**Highly sensitive C reactive protein**

CONTENTS

ABSTRACT

Background

Concomitant thyroid and heart disease are frequently encountered in clinical practice. There are many studies evaluating thyroid function in acute critical conditions. Information on sick euthyroid in myocardial infarction (STEMI&NSTEMI) is limited; its correlation with short and long-term outcome is not fully known.

Methods

100 Patients admitted at ICU with diagnosis of myocardial infarction were included in the study. Myocardial infarction was diagnosed based on electrocardiographic changes with lab evidence of myocardial damage. Thyroid hormone levels (TSH, fT3 ,rT3, fT4) were measured on day 1, 4, 7, & 30. Known hypo/hyper thyroid patients, patients on anti thyroid medications, were excluded in this study.

Subsequently patients were divided into two groups: Patients with low fT3 and elevated rT3 (sick euthyorid) in one group and patients with normal fT3 and rT3 in another group. The two groups were compared in terms of immediate &long term mortality & morbidity.

Results

Sick euthyroid was commonly seen in patients with AWMI.

ICU and hospital stay was more in sick euthyroid group. P value was significant (<0.001). There was a delayed short term recovery in sick euthyroid group.

Number of patients needing invasive management was (47% in sick euthyroid vs 18% in control group). P value was significant (<0.05). More patients needed invasive management on follow up in sick euthyroid group.

Markers for poor outcome such as depressed ejection fraction was more in the sick euthyroid group compared to control group. P value was significant <0.001. Readmissions & mortality was more in sick euthyroid group. Hence patients in sick euthyroid group had increased long term morbidity.

Conclusions

Thyroid dysfunction, particularly sick euthyroid syndrome, can be used to predict the short term & long term morbidity in STEMI & NSTEMI patients.

Keywords

fT3, rT3, fT4, TSH, STEMI, NSTEMI, sick euthyroid syndrome.

INTRODUCTION

INTRODUCTION

Myocardial infarction is one of the major non communicable health hazard. It is an acute event needing critical care with high mortality & morbidity. The incidence of myocardial infarction across the globe is on the rise the reasons being:

a) The lifestyle changes and diet activities have changed over the decade .

b) Higher incidence of diabetes and chronic kidney disease in the population have increased the incidence of CAD.

c) The use of more sensitive markers for diagnosing myocardial infarction.

Every year approximately 1 million patients are admitted with NSTEMI compared to 3,00,000 patients with STEMI. In women the incidence of NSTEMI is more. Male have more incidence of STEMI[(1)].

Mortality data from Global Burden of Diseases Studies have revealed that cardiovascular diseases especially coronary heart disease are important causes of death in India.

In India the incidence of myocardial infarction is 64.37 per 1000[54]. Still one in every 25 cases who survive initial hospitalization die in the 1st year of life. In patients above 75 years of age the rate is approximately four fold high[1].

So the search for markers predicting the poor outcomes in myocardial infarction patients is on the rise.

There is a close relationship between thyroid hormone levels and risk of cardiovascular diseases since they play a major role in the maintenance of cardiovascular system function and hemodynamics. A slight change in thyroid status affects ventricular function, heart rate and rhythm, and increases risk of cardiovascular mortality .

Factors promoting increased cardiovascular diseases are:

[1] Regulation of cardiac contractility through several genes encoding important structural and functional proteins in the myocardium .

[2] Both hypothyroidism and hyperthyroidism individually have been associated with increased risk of coronary artery disease .

[3] Thyroid hormones also has been associated with the risk factors of cardiac diseases like arterial hypertension, atherosclerosis and dyslipidemia.

Thyroid dysfunction can be grouped as hypothyroidism, hyperthyroidism, subclinical hypo &hyperthyroidism. Non thyroid illness affecting thyroid function is SICK EUTHYROID SYNDROME.

It is characterized by decrease in fT3, total T3 & increase in rT3 with normal T4,TSH. This condition is seen in various non cardiac illness such as starvation, sepsis, chronic illness, trauma ,malignancy. Cardiac conditions include heart failure, acute coronary syndromes.

In myocardial infarction haemodynamic disturbances, hypoxia are most important predisposing factors for sick euthyroid syndrome.

Mechanism for these changes include impaired regulation of secretion, decreased peripheral conversion, & altered metabolism.

fT3 is the biologically more active hormone. It has 10 times more affinity to bind with thyroid receptor.

Normally T3 has an increased effect on heart rate, contractility, vascular resistance and oxygen consumption.

In an energy conserving state like myocardial infarction, these low fT3 effects on heart were initially considered as an adaptive mechanism to decrease the cardiac workload.

But various studies had now shown that this condition was rather harmful than having beneficial effects and hence had a significant influence on the short term and long term cardiac events in patients with MI.

So the aim of our study is to use this SICK EUTHYROID SYNDROME as a marker to predict the short and long term morbidity & mortality in patients with STEMI AND NSTEMI .

AIM
OF THE STUDY

AIM OF THE STUDY

To ascertain whether fall in fT3 and elevated rT3 in myocardial infarction patients could be an early indicator of the severity of myocardial infarction and its outcome.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Definition

Myocardial infarction is defined as a clinical syndrome characterised by evidence of ischaemia and combination of evidence of myocardial necrosis on biochemistry, electrocardiographic, and imaging modalities. It comes under the broad classification of ischemic heart diseases.

ISCHAEMIC HEART DISEASE

A. Chronic Stable Angina b. Acute Coronary Syndrome

Based on biochemical markers and ECG changes acute coronary syndrome is further classified as

1. Unstable Angina
2. Non ST Elevation Myocardial Infarction (NSTEMI)
3. ST Elevation Myocardial Infarction (STEMI)

Criteria for the diagnosis of MI: [2]

1) A detection of rise in cardiac troponin with at least one value above the 99th percentile of upper limit. With at least one of the following.

    a) Symptoms of ischaemia.
    b) New significant STEMI, NSTEMI, or New onset LBBB
    c) Pathological q waves on ECG.
    d) Echocardiographic evidence of regional wall motion abnormality.
    e) Angiographic evidence of coronary thrombus.

2) Cardiac death associated with symptoms and ECG evidence of ischaemia but death has occurred before a lab diagnosis of a rise in cardiac markers could be made.

3) PCI related myocardial infarction is characterized by five times rise in troponin values above baseline if baseline is normal or more than 20% rise in troponin values if baseline is elevated and stable. In addition to

    a) Ischemic symptoms
    b) New evidence of STEMI, NSTEMI, or new onset LBBB
    c) Echocardiographic evidence of new regional wall motion abnormality

d) Angiographic evidence associated with procedural complication.

4) Stent thrombosis associated myocardial infarction is detected by either autopsy or angiographic changes in ischemic setting with a rise in troponin levels with atleast one value above 99th percentile.

5) CABG related myocardial infarction is characterized by tenfold rise in troponin values above baseline with evidence of:

a) New pathologic q waves on ECG or new onset LBBB.
b) Angiographic evidence of new graft occlusion.
c) Echocardiographic evidence of new regional wall motion abnormality.

Classification of myocardial infarction[(2)]

Type1: Spontaneous myocardial infarction.
Type2: Myocardial infarction secondary to ischemic imbalance.
Type3: Myocardial infarction resulting in death when markers unavailable.
Type4a: Myocardial infarction related to PCI.
4b: Myocardial infarction related to stent thrombosis
Type5: Myocardial infarction related to CABG.

Causes of myocardial infarction: [2]

Table 3.1 causes of myocardial infarction.

1)	ATHERISCLEROTIC DISEASE.
2)	NON ATHEROSCLEROTIC CAUSES : Arteritis, trauma to coronary arteries
3)	EMBOLI TO CORONARY ARTERIES: Infective endocarditis, prosthetic valve emboli, angiographic complications.
4)	CONGENITAL CORONARY ARTERY ANOMALIES.
5)	MYOCARDIAL OXYGEN DEMAND DISPROPOTION: Aortic stenosis, Thyrotoxicosis, Takotsubo cardiomyopathy
6)	HAEMATOLOGICAL: Polycythemia vera, Thrombocytosis.
7)	MISCELLANEOUS: cocaine abuse.

Pathogenesis of myocardial infarction[2]:

The pathogenesis of STEMI revolves around two factors:

1. **Atherosclerotic plaque formation& factors which potentiate rupture.** The process begins early in life and progresses throughout life with three fates such as

   a) Asymptomatic,

   b) Those producing stable symptoms,

   c) Those that potentiate acute coronary syndromes.

Risk factors for plaque rupture:

- Lipid burden of more than 70%
- Thin fibrous cap are potentially at risk for rupture resulting in acute coronary syndrome.
- Elevated systolic blood pressure.
- Increased heart rate.
- Increased blood viscosity.
- Endogenous (t-pa) activity and plasminogen activating factor 1 levels.
- Coronary vasomotor tone.

Formation of occlusive thrombus

- Initial step is rupture of an unstable plaque with endothelial injury
- Platelet adhesion occurs via attachment of GP 1b to Von Willebrand factor on endothelium.
- Adhesion of platelets to sub endothelial collagen causes activation of platelets.
- The activation causes a change in the configuration of platelet GP 2b-3a receptor.
- This change causes a high affinity for fibrinogen. Fibrinogen can bind two more platelets causing platelet aggregation with cross linking.

- ❖ Activated platelets release ADP and THROMBOXANE A2 which causes further platelet activation releasing more mediators of inflammation.
- ❖ Simultaneously coagulation cascade is activated in a sequential manner and finally fibrinogen gets converted to fibrin under the influence of activated thrombin.
- ❖ This totally occlusive fibrin rich platelet thrombi is the culprit lesion of STEMI patients.

PATHOGENESIS OF NSTEMI

Disproportionate increase in oxygen demand to supply.

The lesions causing such imbalance are

a) Sudden rupture of an unstable plaque with formation of a superficial non occlusive thrombus, with distal embolisation is the commonest cause.

b) Slowly progressive occlusion to a critical level but not completely occluded . This may be the mechanism in post stent restenosis.

c) Dynamic obstruction resulting from spasm of coronary arteries .

d) Conditions such as tachycardia, anaemia, hyperthyroidism, in which the demand of myocardial oxygen increases in a patient with fixed narrowing of an epicardial coronary artery.

But most commonly it is a mixture of above factors causing such a disease.

Pathological classification of infarcts

1) Transmural infarct

It occurs when the entire myocardium is devoid of blood supply with an underlying complete thrombotic occlusion of an epicardial coronary artery.

2) Non transmural infarct

It occurs when the infarct does not involve the entire myocardium but limited to endocardium and intra mural myocardium .This usually occurs after an incomplete obstruction of a coronary artery.

Cellular levels of infarct: [2]

1) Stage of reversibility- ischemia
2) Stage of irreversibility- necrosis.

Table 3.2 reversible ischaemic changes

Time	Microscopic changes
Within 20 min	Decrease in size of glycogen granules ,swelling of mitochondria, sarcoplasmic reticulum,
20 min - 2 hours	Myocyte swelling, development of amorphous densities, relaxation of myofibril and margination of chromatin.

These changes are reversible with reperfusion / thrombolysis.

Subsequently the irreversible changes set in which are of two types:

1) Coagulative necrosis.

2) Necrosis with contraction bands.

RISK FACTORS FOR MYOCARDIAL INFARCTION: [2]

Table3.3 risk factors of MI

Conventional risk factors:	
A)	Smoking & alcohol consumption
B)	Elevated blood pressure.
C)	Elevation of low density lipoprotein (LDL) .
D)	Metabolic syndrome.
Non conventional risk factors:	
A)	High sensitive c- reactive protein (HSCRP).
B)	Homocysteine.

METABOLIC SYNDROME

1) Elevated waist circumference: measured at the top of iliac crest around the abdomen Men — more than 40 inches (102 cm); Women — more than 35 inches (88 cm)

2) Elevated triglycerides: Equal to or greater than 150 mg/dl.
3) Reduced HDL cholesterol: Men < 40 mg/dl. Women< 50 mg/dl.
4) Elevated blood pressure
5) Impaired fasting glucose levels >110mg /dl.

The above mentioned criteria is now modified .

Recently metabolic syndrome is considered as an inflammatory state.& HSCRP is added to the above mentioned criteria.[(2)]

Genetic markers of cardiovascular risk are under development. Of interest being 9p21 allele and PCSK9 gene[(2)].

CLINICAL FEATURES

HISTORY

A) Chest pain: The classical symptom of myocardial infarction is chest pain.

- It can be compressing, squeezing, or choking type of pain.
- The site is retrosternal with anterior spread to both sides predominantly left. The duration of pain is >30 min which can last for several hours.
- Often the pain radiates to jaw, shoulder, upper extremities, along the ulnar border of left arm.
- Aggravated by exertion, relieved by rest or sublingual nitrates.
- The pain is usually associated with nausea, vomiting due to vagal reflex activation.
- Other associated symptoms are diaphoresis, sweating, and a sense of impending doom.

In patients with previous h/o angina pectoris the onset of MI is associated with more intense, prolonged, chest pain not relieved by nitrates.

The pain in MI is due to stimulation of nerve endings in ischaemic area but the necrotic zone or infarct area is usually painless. Thus the presence of pain signifies ongoing ischaemia. Restoration of blood supply to the area relieves pain.

Silent STEMI

Most common among diabetes and it includes a subset of patient who does not have marked symptoms.

They are classified in to two groups

1) One who does not recall any symptoms.
2) The other group who recall some symptoms on leading questions.

Both the groups are identified by q wave in ECG, regional wall motion abnormality, and perfusion defect.

Differential diagnosis of chest pain:

1. **Pericarditis**: Feature to distinguish this pain is radiation to the trapezius ridge which never occurs in ischaemic pain. [(2)]

2. **Pleural pain**: It is sharp, knife like aggravated by respiratory excursions.

3. **Aortic dissection**: Usually tearing pain radiating to back with maximal intensity shorter in duration. Often one or more major arterial pulse is absent.

4. **Costochondritis:** Pain is usually localized and associated with swelling with tenderness.

5. **Gastrointestinal causes:** GERD may mimic myocardial infarction. It is related to meals relieved by antacids.

Other cardinal symptoms are breathlessness, palpitation, syncope.

Table 3.4: Physical Examination

General Appearance	Anxious, restless, gasping for breath.
Heart rate	Rapid, regular tachycardia. But may vary.
Blood pressure	Elevated due to adrenergic drive, hypotension signifies large infarct with LV dysfunction.
JVP	1) Significant in RV infarct. 2) Prominent C-V wave appears with papillary dysfunction. 3) In patients with cardiogenic shock .

Palpation: Usually normal .Features like parasternal heave ,paradoxical s2, systolic thrill may be present depending upon underlying condition

Auscultation

First heart sound: Usually soft during acute phase. Its intensity increases during recovery phase.

Second heart sound: Paradoxical spitting may be seen in those with LBBB or ventricular dysfunction.

Third heart sound: It indicates severity of MI. Those with large infarct and severe LV dysfunction have elevated LV end systolic pressure. Rapid flow during proto diastolic filling of left ventricle causes the third heart sound to be heard in these patients. Also increased flow across mitral valve when mitral regurgitation or ventricular septal defect complicating MI is also a common cause for third heart sound.

Fourth heart sound: it has limited diagnostic value.

Murmurs: A transient or persistent Systolic murmur can be heard.

Table 3.5 Murmurs in MI

Papillary muscle dysfunction	Apical holosystolic murmur with thrill
Septal rupture	Systolic murmur prominent along left heart border
Tricuspid regurgitation	Prominent along right heart border; & increases with inspiration.

LAB INVESTIGATIONS

1) Cardiac enzymes

The myocardial injury causes the circulation of proteins to be released from damaged cells. The detection of these enzymes signifies myocardial injury.

The enzymes used are troponin, myoglobin, CK-MB.

Table 3.6 cardiac enzymes in MI

Enzymes	Clinical importance.
Troponin I & T	It is the most commonly used diagnostic marker. It is commonly not detectable in blood but the level rises more than 20 times in Myocardial infarction. The advantage of this marker is to detect small MI that may be below the detectable level for other markers. Hence this is the preferred marker for diagnosing MI. The level rises 3 hours after onset and persists for 10- 14 days. The diagnosis of acute MI is seen as: 1) A rise of 99th percentile above normal assay. 2) Rise on serial assay, The limitation is its elevation in non cardiac conditions : a) Chronic heart failure. b) Cardiac trauma. c) Pericarditis, myocarditis. d) Post cardiac transplant. e) Stage 4 &5 chronic kidney disease patients.
Creatinine kinase.	It usually rises 3 hours after MI and returns to normal by 48-72 hours. The limitation of this enzyme is its lack of specificity. Several conditions like surgery, defibrillation may cause elevation. The MB isoenzyme has more specificity than CK. A ratio of CKMB mass: CK ratio > 2.5 is significant of MI. The ability to diagnose re infarct due to its short rise and fall has more clinical importance.

The specificity of these enzymes in diagnosing MI is low as it is elevated in non ischemic myocardial events. Thus Electrocardiogram takes a primary role in diagnosing myocardial infarction.

2) ELECTROCARDIOGRAM

The ECG plays an important role in diagnosis of MI.

Based on ST AND T wave changes the MI is classified in to two types.

1) ST elevation MI. 2) NON ST elevation MI.

The serial changes in ECG involving two or more contiguous leads with reciprocal changes in opposite leads are more important.

Criteria to diagnose myocardial infarction:

Table 3.5 diagnostic criteria of MI

ST elevation	Elevation at the J point in two contiguous leads of more than 0.1 mV in all leads other than leads V2-V3. For leads V2-V3 The following cut points apply: ≥0.2 mV in men ≥40 years, ≥0.25 mV in men <40 years, and ≥0.15 mV in women.
ST depression & Twave inversion	New horizontal or down sloping ST segment more than or equal to 0.05 mV in two contiguous leads. T wave inversion of more than or equal to 0.1mV in two leads with prominent r wave or having r/s ratio more than 1.

Table 3.6 diagnosis of MI in patients with LBBB

Concordant ST elevation	> 1mm in the same direction of QRS in leads with a positive QRS complex.(Score 5)
Concordant ST depression	> 1 mm in the same direction of QRS complex in leads V1-V3, where QRS is negative. (score 3)
Discordant ST elevation	> 5 mm in leads in opposite direction of QRS Complex (score 2).

A total score of more than 3 has 90%specificity

Table 3.7: Modified Scarbossa criteria

≥ 1mm of concordant ST elevation in more than 1 leads with positive QRS complex.
≥ 1mm of concordant ST depression in leads of v1-v3with negative QRS complex
ST elevation or depression in the opposite direction of QRS complex that should be >25% amplitude of the preceding S wave.

Table 3.8 leads and MI

Leads involved	Diagnosis of Myocardial infarction.
Septal	V1 and V2
Anterior	V3 and V4
Lateral	V5 and V6
Anteroseptal:	V1-V4
Anterolateral	V3-V6
Extensive anterior	V1-V6.
Inferior	II, III, aVF
High Lateral	I, avL.
Posterior	ST segment depression in V1-V3. ST segment elevation in V7, V8 &V9.

Echocardiography in MI

The use of echocardiogram in diagnosing MI is limited to those patients with new onset chest pain and non diagnostic ECG changes. Demonstration of disordered contraction in these patients can support diagnosis. The role of echocardiogram in prognosis of MI is significant in two situations:

a) Estimated LV function correlates with prognosis of MI.

b) Early use can ascertain viable but stunned myocardium that is a potential indicator of cardiac reserve.

MRI in MI

The use is limited to sub acute and chronic phase rather than acute phase. The advantages of MRI are:

a) It can identify viable and non viable myocardium.

b) It can identify reperfused myocardium.

c) It can identify ventricular chamber characteristics such as size, wall motion, fibrosis and wall thinning.

d) It can differentiate ischemic area from infarction.

e) The gadolinium enhanced MRI can accurately predict the recovery of myocardium post coronary blood flow restoration.

CT angiography in MI: The role of CT angiography in MI is as a non invasive technique to assess the coronary artery thrombus. It is more sensitive than echocardiogram in detecting thrombus particularly in the proximal part of coronary artery.

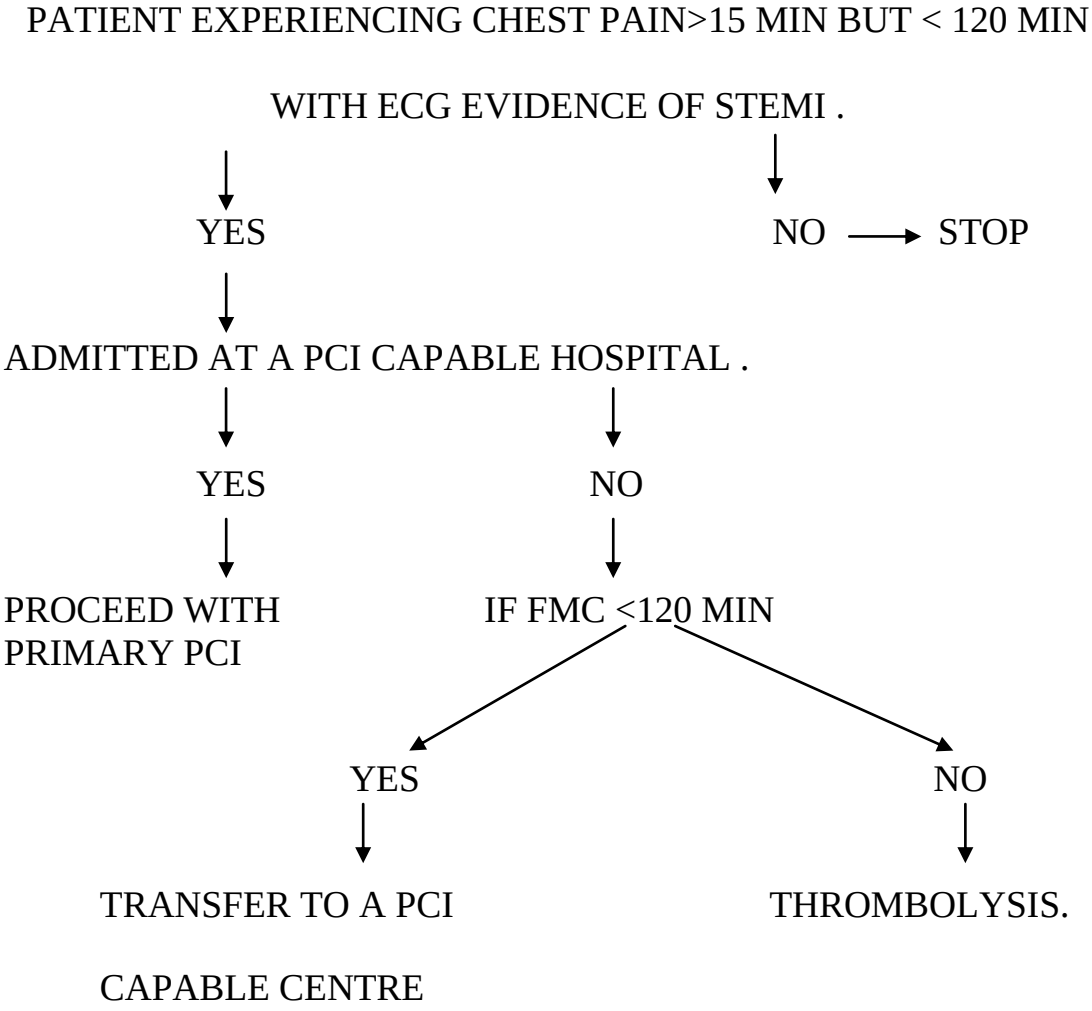
MANAGEMENT

The management algorithm changes according to the pattern of Myocardial infarction and the time of clinical presentation.

ST ELEVATION MI.

STEP 1 : Assessment of the mode of treatment:

3.1 Algorithm of STEMI management



STEP 2: **PCI or FIBRINOLYSIS**

1. If the patient is eligible for PCI, it should be the first choice of treatment.

Two types of PCI:

Primary PCI : PCI is used as a primary reperfusion therapy.

Rescue PCI : PCI done following failed thrombolysis.

Indications for PCI: [2]

- A patient presents within 12 hour of pain onset in a lab with PCI capable.
- Any patient >12 hour pain duration with ongoing ischaemia.
- Presence of cardiogenic shock.
- Contraindicated for fibrinolysis.

The primary goal of PCI is to restore blood flow distal to the obstruction. Assessment of such reperfusion is done by TIMI grading. When assessed after PCI, a successful PCI should obtain TIMI grade 3 flow distally.

Complication

1) Vascular reperfusion injury
2) Stunned myocardium
3) Reperfusion arrhythmias.

The second modality of treatment is FIBRINOLYSIS. They are of two types:

1) FIBRIN DEPENDENT: t-PA, Tenecteplase, Reteplase, Alteplase.

The commonly used drug for fibrinolysis is fibrin dependent agent.

Mechanism of action

The presence of fibrin in clot acts as a scaffold on which the t-PA and plasminogen are bound in such a way that the catalytic effect of t-PA is increased many fold.

Modification of native t-PA has yielded many derivatives which are listed below.[(2)]

Table 3.9 types on fibrin dependent agents:

Agent	Dose	Fibrin specificity	Fibrinogen depletion	Antigenic	Efficacy
Tenecteplase	30mg-<60kg 35mg- 60-69kg 40mg- 70-79kg 45mg- 80-89kg 50mg- >90kg	++++	Minimal	No	85%
Reteplase	Two boluses of 10 units Intra Venous each given 30 min apart.	++	Moderate	No	84%
Alteplase	90min infusion. Bolus : 15 mg IV stat followed by Infusion as :0.75mg/kg for 30 min and 0.5mg/kg for 60 min	++	Mild	No	84%

Dose: Recommended dose is 90 min accelerated regime. It produces better response than a 3 hour fixed infusion.

2) NON FIBRIN DEPENDENT AGENT: Streptokinase

Mechanism of action : Binds with plasminogen and activates but does not need fibrin.

Dose: 1.5 million units iv bolus infusion over 30-60 min.

Side effect: The specific side effect for streptokinase is antigenicity. It is absolutely contraindicated if exposed within 6 months. Hypotension is another side effect.

CONTRAINDICATIONS

ABSOLUTE

- Previous intracranial haemorrhage,
- Cerebral AV malformation.
- Known malignant intracranial neoplasm.
- Aortic dissection.
- Closed head or facial trauma within 3 months.
- Intracranial or spinal surgery within 2 months.
- Active bleeding or bleeding diathesis.
- Ischemic stroke within 3 months .

RELATIVE

- H/O chronic, severe uncontrolled hypertension.
- Blood pressure at initial evaluation>180/110.
- More than 3months H/o ischemic stroke.
- Traumatic or prolonged >10 min CPR.
- Major surgery less than 3 weeks.
- Pregnancy.
- Oral anticoagulant therapy.
- Recent internal bleeding.

Complication of thrombolysis

The only complication of fibrinolytic therapy is bleeding especially intracranial haemorrhage. So the above mentioned contraindications which can potentiate bleeding should be screened before administration

Post thrombolysis management

Indication of CORONARY ANGIOGRAPHY or RESCUE PCI following thrombolysis:

a) Patients with Cardiogenic shock
b) Acute severe heart failure
c) Post infarct angina
d) Patients with evidence of failed reperfusion
e) Evidence of re occlusion.
e) Stable patients –ideally before discharge.

Indication for CABG POST CAG IN STEMI PATIENTS undergoing thrombolysis as primary management :

1) Those who underwent thrombolysis or rescue PCI but still has ischaemic pain.

2) High risk coronary anatomy at initial cath lab evaluation such as left main stenosis.

3) Complicated STEMI such as septal rupture, papillary muscle dysfunction.

Step3: ANTI COAGULATION

HEPARIN

The primary role of heparin administration is to maintain the patency of blood flow in infarct related artery. Secondarily it prevents development of deep vein thrombosis, pulmonary embolism and ventricular thrombus formation.

Mechanism of action:

It prevents thrombosis by inhibiting factor 10 A & thrombin through an anti thrombin dependent mechanism.

Side effect : The major side effect is bleeding.

Risk factors for bleeding include:

- Low body weight
- Female
- Prolongation of activated partial thromboplastin time (>90-100 seconds).

Dosage

Bolus dose of 60 units/kg to a maximum of 4000 units, followed by 12 units per hour/kg to a maximum of 1000 units for a duration of 48 hours . Activated partial thromboplastin time to be adjusted 1.5-2 times the normal.

The infusion duration of >48 hours is associated with increased risk of heparin induced thrombocytopenia. So alternate anticoagulation are preferred in such cases

Disadvantages

- Difficult to administer and unreliable anti coagulation.
- Frequent aPTT monitoring.
- Anti thrombin dependency for thrombin inhibition.
- Inability to inhibit clot bound thrombin.

LMWH

Advantages

1) It has Stable anticoagulant effect
2) High bio availability, so subcutaneous dosing adequate,
3) High factor 10a:2a ratio, thereby blocking the generation of thrombin at a higher step.
4) Less risk of developing HIT.
5) More suitable for prolonged anticoagulation.

Dosage

Enoxaparin

Age<75 years :30 mg iv bolus followed by 1mg/kg 12th hourly

Age >75 years : No bolus. 0.75mg/kg every 12th hourly.

Regardless of age if creatinine clearance <30ml/min: 1mg/kg sc every 24hours.

Direct thrombin inhibitors

Bivalirudin

The use of this agent is on the rise when compared with LMWH or heparin due to its increased benefits in preventing major cardiovascular event with a decreased risk of bleeding. It is approved as first line of anticoagulant in patients treated with primary PCI.

ANTI PLATELETS

All patients with STEMI should receive aspirin unless contraindicated. The dosage should be 162-325mg mg stat followed by 75-162 mg daily. Those who don't tolerate aspirin should be maintained at a lower dose. But the duration of treatment is lifelong.

P2Y12 INHIBITORS

The addition of p2y12 inhibitors is indicated in all STEMI patients. The first prodrug is **Clopidogrel.** Newer drugs are **Prasugrel and Ticagrelor**. The dosing of the drugs is mentioned below:

Table 3.10 p2y12 inhibitors

Agent	Loading dose	Maintenance dose
Clopidogrel: Those who undergo thrombolysis: Age< 75 years. Age >75 years.	 300mg. No loading dose.	75mg for all patients.
Those who undergo PCI: after thrombolysis <24hours >24hours	 300mg 600mg.	
Prasugrel	60mg	10mg.
Ticagrelor	180mg	90mg.

The duration of treatment is 1 year. Prasugrel is contraindicated in patients with history of cerebrovascular disease.

Step 4

General measures : The general measures are aimed at decreasing cardiac pain. It is usually achieved with a combination of analgesics and vasodilators.

Analgesics: Morphine remains the drug of choice. Dose is 4 to 8mg iv stat and dose of 2 mg at 5-15 min intervals. Hypotension, vomiting, respiratory depression should preclude further use.

Oxygen: Patient with STEMI and hypoxemia should receive oxygen supplementation.

Nitrates: They are indicated in all CAD patients due to their ability to augment coronary blood flow. It is administered through sublingual route. Contraindicated in patients with hypotension and right ventricular infarction.

Step 5: Pharmacological therapy:

1) **Beta blockers**: All STEMI patient should receive beta blockers within the first 24 hours if not contraindicated. The addition of beta blockers has both immediate and long term benefits.

The immediate benefit is due to its reduction in heart rate, cardiac index and Blood pressure. There by the oxygen demand to supply mismatch is reduced. This reduces symptoms of further ischaemia.

Contraindication:

- Signs of heart failure or low output.
- Heart block.
- Systolic blood pressure < 120mmHg;
- Sinus bradycardia.
- Asthma or reactive airways.

The commonly used beta blockers include Metaprolol, Bisoprolol, Carvedilol and Atenolol.

Inhibition of RAAS system:

The use of ACE/ARB group of drugs is recoommended in all STEMI patients. By preventing ventricular remodeling, haemodynamic changes, and reduced incidence of heart failure it plays a vital role in MI patients. The commonly used drugs are Ramipril, Enalapril, Losartan and Telmisartan.

Side effects

1. First dose hypotension,
2. Cough,
3. Angioedema,
4. Hyperkalemia
5. Cardiogenic shock.

OTHER DRUGS

1. Aldosterone antagonist.
2. Mineralocorticoid receptor antagonist.

INDICATIONS OF ALDOSTERONE ANTAGONIST IN MI:

1. EF <40%.
2. Patients with diabetes.
3. Patients with heart failure

The commonly used drugs are aldactone and eplerenone at a dosage of 25mg up to a maximum dose of 50mg. The prerequisite before using the drug is creatinine clearance>30ml/min and potassium<5meq/l.

The serious side effect of this group of drugs is hyperkalemia especially when combined with ACE inhibitors.

Nitrates

Nitrates are preferred in acute MI because of its ability to

- Decrease preload.
- Reduce wall tension.
- Increase coronary blood flow.

Prolonged use of these drugs is needed in those with recurrent ischemia and with failure symptoms. In asymptomatic patients it is not used beyond first 48 hours. Tolerance, hypotension, tachycardia are the side effects.

Magnesium

A fall in serum magnesium may develop in STEMI patients. Due to the risk of developing arrthymias, it should be monitored periodically and if decreased replenished. Serum concentration of 2 meq/l or greater is maintained.

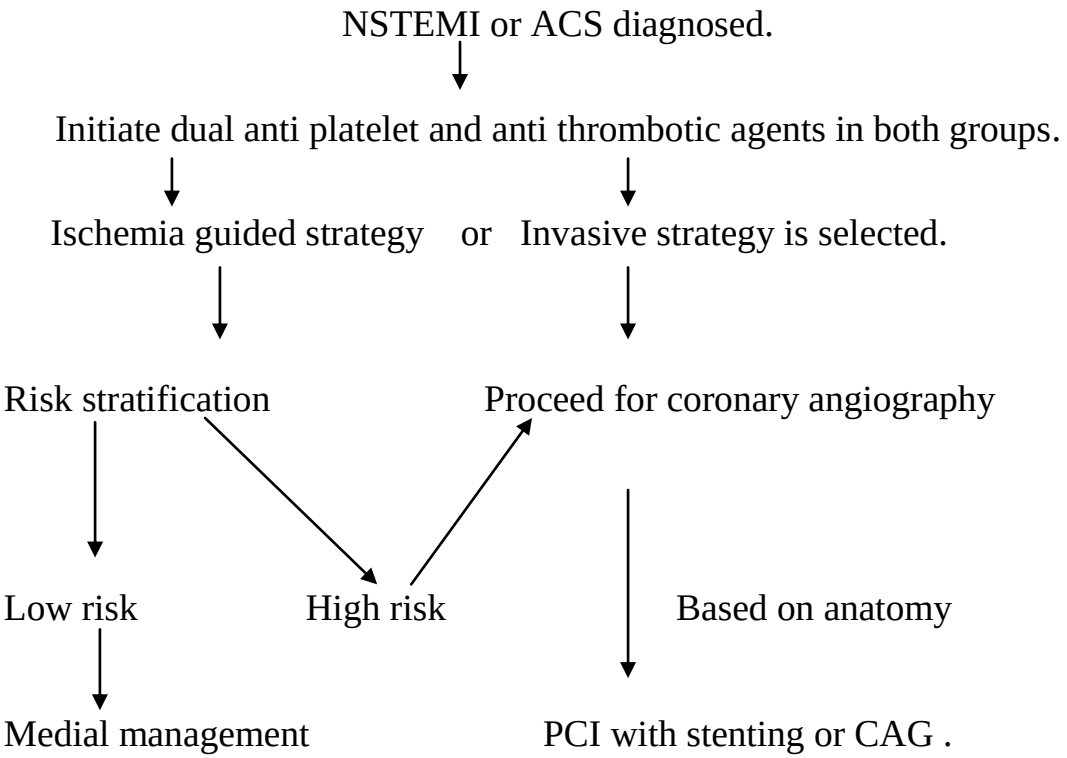
MANAGEMENT OF NSTEMI

The management of NSTEMI differs from STEMI by the following ways.

a) There is no role of fibrinolysis in NSTEMI.

b) The initial goal of treatment is to restore blood flow and plaque stabilization using anti platelets and anti thrombotic agents.

Algorithm 3.2 of NTEMI management:



INDICATIONS FOR INVASIVE STRATEGY:

1) Recurrent angina or early post infarct angina.

2) Development of New ST segment depression.

3) Ejection fraction <40%.

4) Sustained ventricular arrthymias.

5) Mild to moderate renal dysfunction.

6) Prior PCI<6months and post CABG status.

7) Diabetes mellitus.

8) Grace score more than109 and TIMI score more than 2.

9) Symptoms of worsening heart failure or new onset mitral regurgitation.

INIDCATIONS FOR ISCHEMIC STRATEGY

1) Grace score less than 109.
2) Patient or clinician preference in absence of high risk features.
3) Low risk stratification by non invasive imaging.

Risk stratification among ischaemic stratergy patients

- Treadmill exercise testing is useful in patients able to exercise in whom the ECG is free of resting ST changes that may interfere with interpretation.

- Patients with an ECG pattern that would interfere with interpretation of the ST segment (baseline ST abnormalities, bundle-branch block, LV hypertrophy with ST-T changes, intra ventricular conduction defect) should have an exercise test with imaging.

- Pharmacological stress testing with imaging is recommended when physical limitations preclude adequate exercise stress.

- A noninvasive imaging test (ECHO) is recommended in all patients to evaluate LV function in patients with definite ACS.

Table 3.11 drugs used in NSTEMI

Analgesia: Morphine
Anti ischaemic dugs: Nitrates, Beta blockers, Calcium channel blockers.
Anti platelets: Aspirin, Clopilet, Ticagrelor , Prasugrel.
Gp2b3a inhibitors: Eptifibatide, Tirofiban.
Anticoagulants: Unfractionated heparin, Low molecular weight heparin Fondapaurinox, Bilavirudin.

COMPLICATIONS OF MI

a) Haemodynamic disturbances.

- Mechanical causes.
- Left ventricular failure.
- Cardiogenic shock.

b) Arrhythmias.

1) Mechanical cause

Table 3.11 mechanical complications of MI[(2)]

Characteristic	Septal rupture	Rupture of free ventricular wall	Papillary muscle rupture.
Onset	Bimodal; <24 hours to 3-5days.	Bimodal ; <24 hours to 3-5days.	Bimodal ; <24 hours to 3-5days.
Clinical manifestation	Chest pain, shortness of breadth, Hypotension.	Pleuritic Chest pain, syncope, hypotension. Arrthymias, Sudden death.	Abrupt onset of shortness of breath and pulmonary edema with hypotension.
Physical findings	Holosystolic murmur with thrill, s3gallop, Accentuated second heart sound.	JVP elevated, Pulsus paradoxus, kussmaul sign	Severe pulmonary edema with cardiogenic shock.
Echocardiography findings	Left to right shunt on colour doppler with RV overload	>5mm pericardial effusion with high acoustic echoes within the pericardium and features of cardiac tamponade.	Torn papillary muscle or leaflet with severe mitral regurgitation.
Right heart catheterisation	Increase in O2saturation from right atrium to right ventricle.	Equalization of diastolic pressure in cardiac chambers.	No increase in oxygen saturation seen

2) Left ventricular failure

It is the single most predictor of mortality in patients with MI. It can be of two types systolic and diastolic dysfunction. The systolic dysfunction is associated with an increase in pulmonary capillary pressure and decreased cardiac output. Clinical manifestation increases as injury to ventricle increases.

Killip has classified in to four classes based on clinical features of left ventricular failure. Each class is associated with varied clinical outcome.

Table 3.12 : Killips classification &outcome

Class I: no signs of heart failure.	6%. Mortality
Class II: patients with rales, cracles, s3,elevated JVP.	17% Mortality
Class III: patients presenting with acute pulmonary edema.	38%. Mortality
Class IV: patients with Cardiogenic shock or hypotension.	81%. Mortality

The management of LV failure depends on two factors

a) Drugs that reduce preload - ventricular filling pressure.

b) Drugs that reduce afterload- systemic resistance & improve contractility.

a) Diuretics

Intravenous Furosemide is a potent diuretic drug given at doses of 20-40 mg repeated at 4^{th} hourly interval. It causes pulmonary capillary vasodilation with a fall in capillary wedge pressure& decreases preload. Thus the left ventricular diastolic volume and pressure decreases. This leads to increase in cardiac output, stroke volume and ejection fraction. The decrease in preload also augments coronary blood flow thereby decreasing the demand.

b) Vasodilators

These drugs increase cardiac output by both decrease in peripheral resistance and decrease in intraventricular filling pressure. Both these mechanisms promote cardiac output and prevent rise in pulmonary capillary wedge pressure. The commonly used drugs are nitroglycerine and sodium nitroprusside.

Dose

Nitroglycerine: 5mcg/min q 3-5 min up to 20mcg/min, until relief of pain or haemodynamic improvement is achieved. Not contraindicated in renal failure

c) Beta agonist

These drugs act by predominantly increasing the force of contraction. They are used when

- Cardiac index less than 2.2 L/Min,
- Pulmonary capillary wedge pressure more than 24mmhg, despite diuretics and dilator therapy.

Drugs used are dopamine, dobutamine and norepinephrine.

Dopamine: The positive ionotropic action and vasodilatory properties of dopamine increases cardiac output and tissue perfusion. Dose: 5-15mcg/kg/min.

Dobutamine: It has a positive ionotropic effect. It can be administered at a dose of 2-20 mcg/kg/min not exceeding 40mcg/kg/min.

Norepinephrine: It is used widely as first line in cardiogenic shock at a dose of 8-12mcg/kg/min. Maintenance dose:2-4 mcg/kg/min.

All these agents cause tachycardia, prone for ventricular and supraventricular arrthymias.

Milrinone: It is a non catecholamine ionotropic with vasodilator property. Loading dose of 0.5mg/kg/min given over 10 min followed by 0.37-0.75mg/kg/min. Hypotension is a common side effect.

Cardiogenic Shock

It is the more severe clinical form of left ventricular failure. It is characterized by persistent hypotension for more than 30 minutes[(2)] with

- Systolic BP less than 90mmHg.
- Cardiac index less than 2.2 L/Min.
- Pulmonary capillary wedge pressure more than 18mmHg.

Patients Prone for cardiogenic shock include:

- History of diabetes.
- Old age.
- Previous MI.
- Anterior wall involvement.

Management

Ionotropes and vasopressor agents. All those who worsen with medical management need mechanical support such as intra aortic balloon counterpulsation and ventricular assisted devices.

ARRHYTHMIA

Table 3.13 showing arrhythmias & management

Category	Arrthymias	Treatment
Electrical instability	VT& VF VPC AIVR	Defibrillator cardioversion. Lignocaine, amiodarone. Beta blockers. Usually benign. Atropine or Atrial pacing.
Pumpfailure/ symphatetic stimulation.	Atrial flutter/fibrillation Paroxysmal SVT	Digitalis, Amiodarone, Verapamil. Vagal stimulation, Betablockers,
Bradyarrthymias	Junctional escape rhythm Atrioventrcular &intraventricular block.	Atropine, atrial pacing. Atrial pacing.

Pericarditis

It is common up to 8 weeks following MI. It typically produces a pain mimicking MI. The distinguishing feature is radiation to the trapezius ridge. Worsens on deep inspiration, relieved when patient sits or leans forward. It manifest as pericardial friction rub. Treatment is aspirin 650mg every 4^{th} hourly. Steroids and NSAIDs are avoided.

Pericardial effusion

Effusions are generally associated with large MI and anterior wall MI & detected by echocardiography. The resolution of effusion takes months as reabsorption is slow. Haemorrhagic effusion indicates ventricular rupture.

Dresslers syndrome

Pericarditis occurring between 1 to 8 weeks following MI. Manifest as fever, pericardial effusion, elevated ESR, leucocytosis. Usually autoimmune in pathology. Treatment is aspirin.

PHYSIOLOGY OF THYROID HORMONES

Triiodothyronine (T3) and Tetraiodothyronine (T4) are the two principal hormones produced by thyroid gland in our body. Initially iodine is absorbed in the gut and is converted to iodide and transported in the blood. It is then actively transferred into the thyroid cell by “Iodide trapping”.

The trapped iodide is “Oxidized” to iodine and combines with tyrosine to form Mono iodotyrosine (MIT) and Diiodotyrosine (DIT) respectively.

Oxidation, iodination and coupling reactions are catalyzed by “Thyroid per oxidase”. Thyroid hormone thus produced is bound with thyroglobulin until secreted.

There are two biologically active thyroid hormones:

- Tetraiodothyronine (T4; usually called thyroxine)
- Triiodothyronine (T3) Derived from modification of thyroxine.

Once secreted in the blood, it is transported in two forms. T4 is predominately bound to thyroid binding globulin whereas T3 is predominatly bound to albumin. The other form is free T3 and T4. These free forms are in equilibrium with bound form.

The thyroid secretes about 80 microgram of T4, & 5 microgram of T3 per day about 20% of circulating T3. Rest of T3 is derived from peripheral deiodination of T4 by deiodinise enzyme 1&2. This conversion takes place mainly in the liver and kidneys. The T3 formed is then released to the blood stream. rT3 is also derived from T4 by deiodinase enzyme 3 in equal amounts to free T3.

Control of thyroid hormones

Regulation of thyroid hormones is at various levels

1. Hypothalamus
2. Pituitary
3. Thyroid gland
4. Cellular level.

Thyroid hormone receptor physiology

They are members of large family of nuclear receptors similar to steroid hormone receptors. They function as hormone-activated transcription factors and thereby act by modulating gene expression. Till now four isoforms namely alpha1,alpha2,beta1,beta2 have been isolated.

Thyroid hormone receptors have three functional domains:

1) Transactivation domain.
2) Ligand binding and dimerization domain.
3) DNA-binding domain which binds with promoter sequences such as hormone responsive elements.

In the inactive state, the transactivation domain forms a hetrodimer with RXR and assumes a state of inactivation. Once thyroid binds to the

ligand binding site it undergoes dimerization and becomes active. On activation, it binds to the adjacent DNA promoter sequences and activates them.

Thyroid hormone receptors are found in many tissues of the body, but not in adult brain, spleen, testes, uterus, and thyroid gland itself.

T3 has a much greater affinity & biological activity (about 10 X) than T4. rT3 has 1% of activity of T3 . Hence acts as a antagonist binding to T3 receptors. The ratio of f T3: rT3 is 3.3:1. Conditions that decrease T3 &increase rT3 blocks the action of action of T3 on its receptors.

Effects of T3 on heart

1) Thyroid hormone has a positive chronotropic effect, & increases per gm oxygen consumption of heart.[53]

2) Erythropoietin secretion is upregulated by thyroid hormone. This increases the red blood cell mass and the total blood volume. Thus it increases cardiac preload.[53]

3) The thyroid hormone directly promotes arterial smooth muscle relaxation causing reduction in systemic vascular resistance. This reduces afterload .

Thus thyroid hormones increase heart rate, preload, oxygen consumption per min per gram of cardiac tissue. All these corresponds to an increased workload on heart.

Myocardial infarction and thyroid hormones

Thyroid hormone as mentioned earlier is a catabolic hormone. In conditions like myocardial infarction where already there is a demand supply mismatch, body adapts itself to such a condition by decreasing thyroid hormone levels.

Hence such a decrease in thyroid hormone levels is a frequent observation and is considered as an energy adaptation to acute stress[21]. Previously it was thought that this is a beneficiary adaptive mechanism in a failing heart.

But various researchers have now studied the adverse events of such alteration in hormonal changes.

Such an alteration in thyroid function due to non thyroid illness is described as **"Sick Euthyroid Syndrome" (SES).** It is characterized by low T3 and/or free T3, increased reverse T3 (rT3) and normal TSH, T4 and free T4 levels[5]. Since patients with this syndrome do not exhibit symptoms of hypothyroid, it is considered as an acute event.

PATHOPHYSIOLOGY OF SICK EUTHYROID SYNDROME

Inflammation, Hypoxia and Hemodynamic instability are considered to be the predisposing factors [12].

Factors promoting low T3 levels: [21]

1. Impaired peripheral deiodination

Inflammatory mediators such as IL-6 decreases the peripheral conversion of T4 to T3 resulting in low fT3 levels. IL-6 inhibits type 1 deiodinase activity[12]. Type 1 deiodinase is responsible for peripheral conversion of T4 to T3. Thus the serum level of T3 is decreased.

At the same time, IL-6 can increase the transcription of deiodinase3 protein by activating the JAK/STAT pathway which causes increased synthesis of rT3.[12

Hypoxia in peripheral tissues is another factor contributing to the low fT3 levels. Increased hypoxia-induced factor-1 activates deiodinase3 protein in tissues, which might contribute to lowering the fT3 level by increased synthesis of rT3.

2. Decreased thyroid releasing hormone

(i) Failure of hypothalamo pituitary axis response to decreased serum T3 concentration.

(ii) Suppressed TRH&TSH secretion due to normal or slightly elevated serum T4.

3) Reduced thyroid receptor expression in heart is another factor is another way by which the thyroid action is decreased in acute conditions

EFFECTS OF LOW fT3 ON HEART

Short term

The contractile ability of the heart is influenced by thyroid through calcium handling, ion channels and contractile proteins[12]. When it is down regulated in AMI, intracellular calcium handling is affected leading to calcium overload within the cell causing myocardial stunning with Systolic Dysfunction [12].The increase in systemic vascular resistance in

low thyroid state leads to increased cardiac workload predisposing diastolic dysfunction[7].This leads to reduction of cardiac output and subsequently left ventricular ejection fraction is reduced manifested as symptoms of acute ventricular failure to cardiogenic shock. .

Long term

Long term effects include changes in the transcription of many structural and functional cardiac genes.

1) A low thyroid hormone state decreases α-myosin heavy chain (α-MHC) and sarcoplasmic reticulum calcium-activated ATPase (SERCA2) mRNA expression and increases β-MHC and phospholamban (PLB) mRNA expression.[12]

2) A low thyroid hormone state suppresses the pro-survival PI3K/AKT signaling pathway and activates the pro-death P38/MAPK signaling pathway in cardiac cells following ischemia.

All these changes predisposes to VENTRICULAR REMODELLING. It is characterized by an irreversible decrease in effective contractility with decreased ejection fraction,and ventricular dilatation leading to various complications such as post infarct failure and arrthymias.

Ioannis Lymvaios et al [13] conducted a study on thyroid hormone and recovery of cardiac function in 47acute myocardial infarction patients. They used echocardiography as a tool of left ventricular function recovery and correlated with fT3 levels. They found a positive correlation between fT3 levels with early and late recovery of cardiac function.

Kazım Serhan Özcan et al [4] conducted a prospective study on patients admitted with myocardial infarction. Immediate angiography was done and patients underwent stent or balloon angioplasty. Simultaneously thyroid hormones were measured. Patient was followed up for a period of 15 months and was observed for adverse cardiac events during the initial stay in hospital and follow up. The main finding of their study was that both in-hospital and long term mortality were higher in the low fT3 group. Subgroup analysis revealed that these results were mainly driven by the high rates of mortality in patients with sick Euthyroid syndrome.

Friberg et al[9] conducted a study measuring reverse T3 levels of 331 patients with myocardial infarction. Increased reverse T3 levels were found to be related to increased 1-year mortality.

Lazzeri et al[10] conducted a study on 641 STEMI patients, and studied the in-hospital mortality of the sick euthyroid group. The patients in this study were treated with PCI. The failure of intervention and

mortality was observed to be higher in patients with sick euthyroid syndrome.

Molinaro et al[25] followed 1026 patients with acute cardiac diseases for 30 months after diagnosis. Cardiac mortality was found to be higher in the group with subclinical hypothyroidism and sick euthyroid syndrome indicating the prognostic implications of thyroid hormone levels on long-term adverse cardiac events.

Shilpa Deoke et al [21] in a study conducted at Nagpur correlated the ejection fraction with sick euthyroid syndrome in acute state and found patients with sick euthyroid syndrome had an EF<40%. 100% of patients with cardiogenic shock had low ft3 levels. Hence the acute correlation between thyroid and severity of myocardial infarction was studied.

J Adawiyah et al [5] conducted a study on association between acute coronary syndromes and thyroid hormones. This was one of the few studies that included unstable angina patients. All patients were followed up for a period of 6 months. Number of readmissions, arrthymias and cardiac failure were observed among two groups sick euthyroid and control group. Statistically significant difference was observed. Sick euthyroid group had more morbidity.

Edita Jankauskien et al [11] conducted a study where acute myocardial infarction patients were divided in to two groups based on fT3 levels taken on 0,4, &7 days. Echocardiography was done. Patients on the low fT3 group had a significant low ejection fraction.

Baowei Zhang et al [12] conducted a study on 500 STEMI patients and were classified in to two groups based on fT3 levels. Patients were followed for a period of one year with mortality and adverse cardiac events as comparing indicators among the two groups. They observed that a low fT3 level in patients with acute myocardial infarctions was a strong predictor of short-term and long-term poor prognosis.

In the above mentioned studies the indicators taken for studying the effect of sick euthyroid were either mortality, adverse cardiac events like failure, arrthymias or echocardiography. In our study all the factors were taken together and the prognostic significance of thyroid hormones on myocardial infarction was studied.

MATERIALS AND METHODOLOGY

MATERIALS AND METHODS

STUDY TITLE: To study the role of fT3 AND rT3 in predicting the mortality and morbidity in STEMI AND NSTEMI patients.

AIM OF THE STUDY: To ascertain whether fall in fT3 and elevated rT3 in myocardial infarction patients could be an early indicator of the severity of myocardial infarction and its outcome.

OBJECTIVES

1) PRIMARY OBJECTIVES

At the time of admission:

A) Immediate mortality in both groups.

B) Number of Patients requiring immediate intervention like PCI/CABG .

C) Duration of ICU and hospital stay in both groups

At the end of first, fourth, seventh month and one year follow up of both Groups:

A) Mortality of cardiac illness.

B) Morbidity indicators like:

a) Patients requiring intervention like CABG/PCI

b) Readmission for following cardiac complications:

1. Arrhythmias.

2. Post infarct angina,

3. Post infarction failure.

2) SECONDARY OBJECTIVES

At the time of admission

A) ECG changes .

B) Echocardiographic changes

At the end of first, fourth, seventh month and one year :

A) Persistence of ECG changes.

B) Echocardiographic changes.

STUDY CENTRE: ESIC Medical college & PGIMSR, KK nagar,Chennai-78.

DURATION OF STUDY: 12 months

STUDY DESIGN: Analytical, longitudinal study

STUDY POPULATION: This study was conducted among 100 patients admitted at ICU in ESIC Medical college Hospital, KKnagar, chennai with the diagnosis of myocardial infarction based on clinical , ECG and lab evidence.

Patients were taken up for study after informed consent .Cases that are taken up for study are classified in to two groups based on serial fT3 &rT3 measurements on day1,4,7.&30 respectively.

Group A has patients with low fT3&elevated rT3 & group B with normal fT3 &rT3 levels. Both fT3&rT3 are measured by ELISA chemiluminesence methods.

INCLUSION CRITERIA : All patients with new onset acute STEMI and NSTEMI admitted at ICU .

EXCLUSION CRITERIA

1. Primary hypothyroidism and hyperthyroidism.
2. Coronary revascularisation within 6 months
3. Major surgical procedures within 6months.
4. Therapy with amiodarone, lithium ,iodinated contrast within 2 weeks.
5. Chronic renal failure patients.
6. Valvular/ congenital heart disease.
7. Established thyroid neoplasia.
8. Clinical evidence of sepsis or cachexia.
9. COPD on Antibiotics

METHODOLOGY

100 newly diagnosed consented myocardial infarction patients admitted at ICU will be taken up for study.

↓

ECG changes of ST segment elevation or ST segment depression in contiguous leads or new onset LBBB with labaratory evidence of myocardial damage will be taken as diagnostic criteria.

↓

Detailed history and clinical examination will be made

↓

Routine lab investigations is done for all patients.

↓

5ml of venous blood sample will be collected on day 1, 4 7 &30 respectively.

TSH, fT4, fT3& rT3 will be measured by chemiluminesence method.

Based on the fT3 &rT3 patients will be grouped as

GROUPA	GROUPB
50 Patients with low fT3& elevated rT3	50 MI patients with normal T3&rT3

At the time of admission:

GROUP A	GROUPB
Mortality	Mortality
Number of patients requiring PCI/CABG	Number of patients requiring PCI/CABG.
Duration of ICU/HOSPITAL stay	Duration of ICU/HOSPITAL stay .
Echocardiographic changes	Echocardiographic changes
ECG changes	ECG changes.

At the time of 1st, 4th ,7th &12th month follow up:

GROUP A	GROUPB
Mortality	Mortality
Number of patients requiring PCI/CABG	Number of patients requiring PCI/CABG.
Duration of ICU/HOSPITAL stay	Duration of ICU/HOSPITAL stay.
Echocardiographic changes	Echocardiographic changes
Persistence ofECG changes	Persistence of ECG changes.
Number of times readmission for the following cardiac events 1) Arrhythmias. 2) Reinfarction &post infarct angina 3) Post infarct failure	Number of times readmission for the following cardiac events 1) Arrhythmias. 2) Reinfarction&post infarct angina 3) Post infarct failure

The final data was entered onto Microsoft excel sheet 2007version and statistical analysis was done using SPSS software. The statistical tools applied were mean, median, standard deviation, chi-square, student t-test. The results are considered to be very significant if p value <0.001 and significant if p value <0.05.

RESULTS
AND
ANALYSIS

OBSERVATION AND RESULTS

Table 5.1: Age distribution

Age (years)	Group A N%	Group B N%	Total N%
31-40	3(6%)	6(12%)	9(9%)
41-60	34(68%)	33(66%)	67(67%)
>60	13(26%)	11(22%)	24(24%)

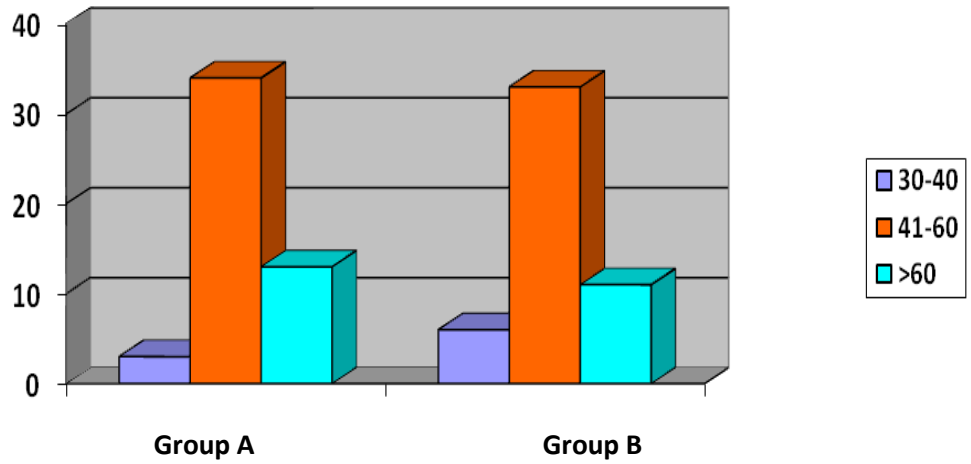


Figure 5.1 AGE distribution

Interpretation

Mean age group in group A was 55.14 years and group B was 52.60 years . P value was >0.05 which was not significant ,i.e age distribution among both the groups were equal

Table 5.2: Sex Distribution

Sex	Group A N(%)	Group B N(%)	Total N(%)
Male	31(62%)	33(66%)	64(64%)
Female	19(38%)	17(34%)	36(36%)

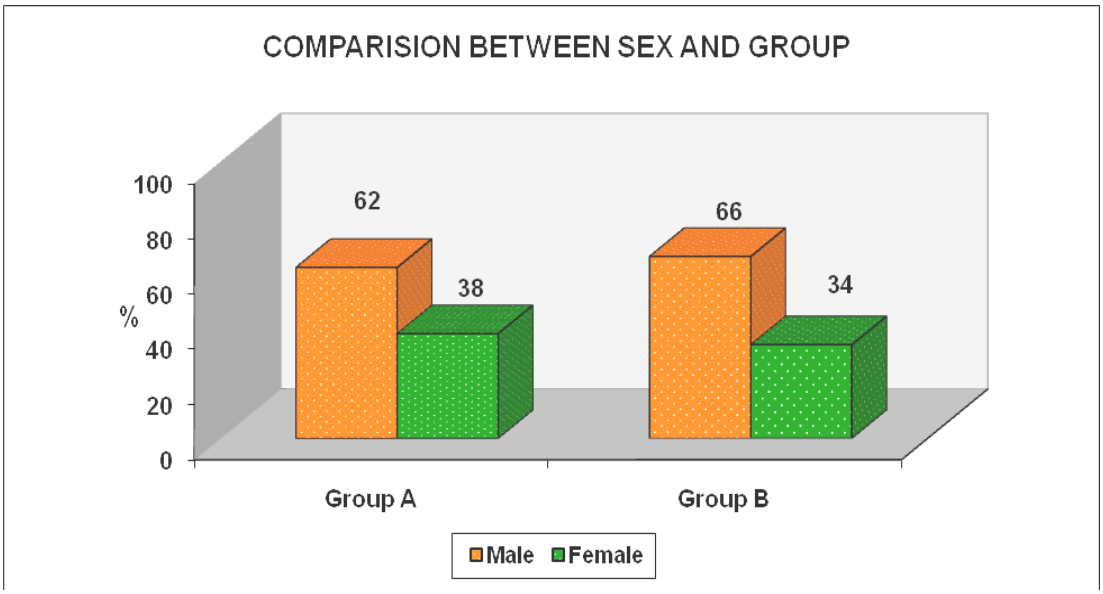


Figure 5.2 Sex distribution

Interpretation

Majority of study subjects (64%) were males while the remaining 36% were females .p value was 0.677 which is not significant ie sex distribution among both the groups were equal.

Table 5.3: TSH levels

TSH	Group A		Group B	
Day	Mean (mIU/L)	S.D	Mean (mIU/L)	S .D
1	2.95	0.59	2.93	0.58
4	2.94	0.60	2.95	0.59
7	2.92	0.60	2.94	0.59
30	2.92	0.59	2.94	0.58

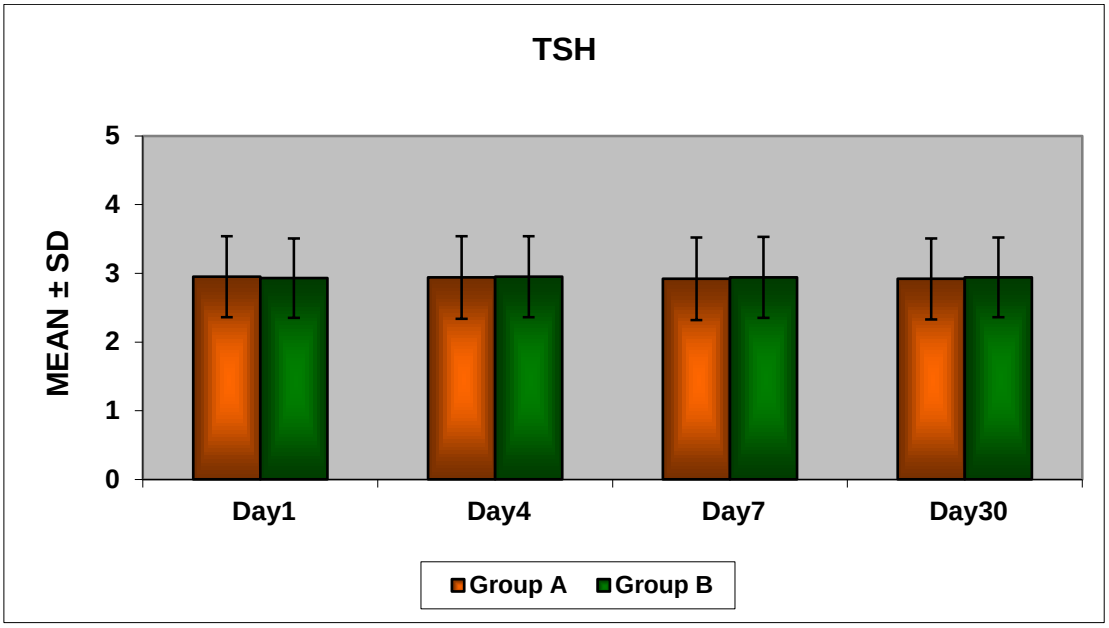


Figure 5.3 TSH levels

Interpretation

No difference in TSH values were observed in both the groups p value(>0.05).

Table 5.4 : fT4 values

f T4	Group A		Group B	
Day	Mean (ng/dl)	S.D	Mean (ng/dl)	S .D
1	1.44	0.28	1.44	0.26
4	1.42	0.27	1.63	0.37
7	1.42	0.26	1.42	0.25
30	1.38	0.34	1.44	0.25

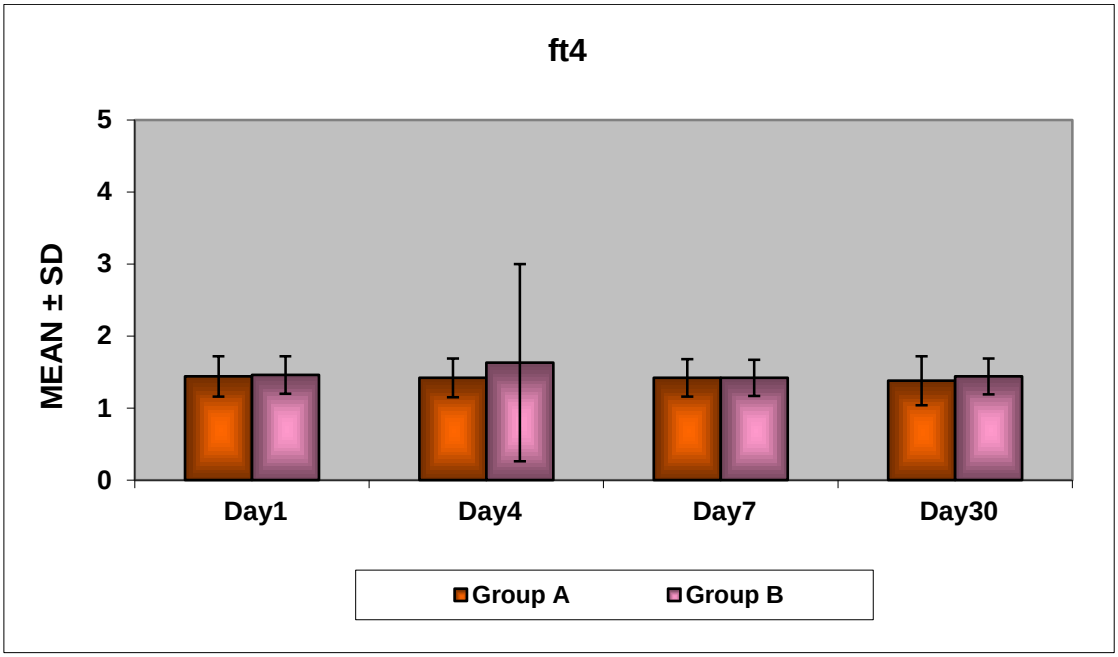


Figure 5.4 fT4 values

Interpretation

No difference in fT4 values were observed in both the groups (p value>0.05).

Table 5.5: fT3 day1 levels.

Day 1	Group A	Group B
Mean (pg/ml)	3.40	3.40
S.D	0.45	0.31
P value	>0.05	

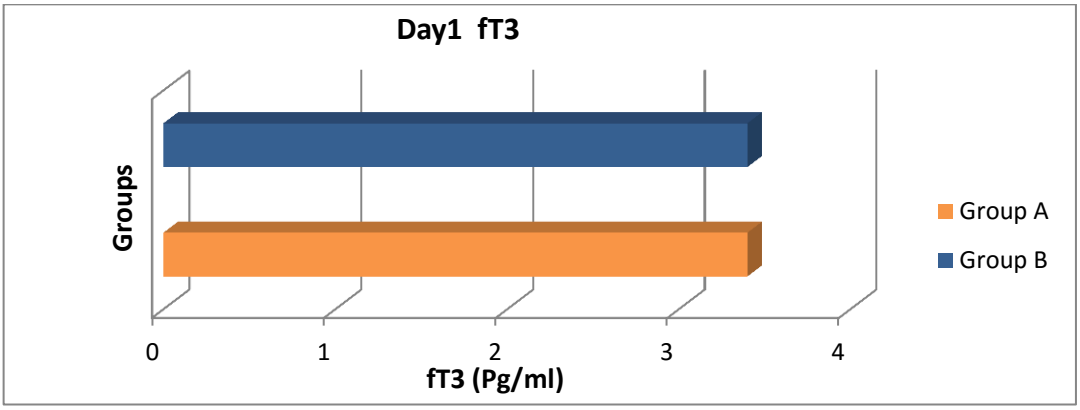


Figure 5.5 fT3 day 1 values

Table 5.6 fT3 day 4 levels

Day 4	Group A	Group B
Mean (pg/ml)	2.31	3.33
S.D	0.47	0.28
P value	<0.001	

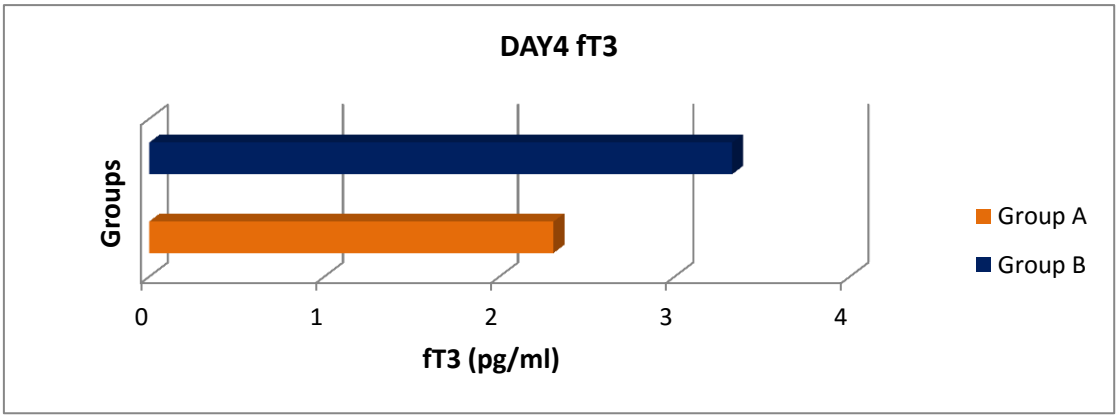


Figure 5.6 fT3 day 4 values.

Table 5.7 fT3 day 7 levels.

Day 7	Group A	Group B
Mean (pg/ml)	1.87	3.31
S.D	0.46	0.28
P value	<0.001	

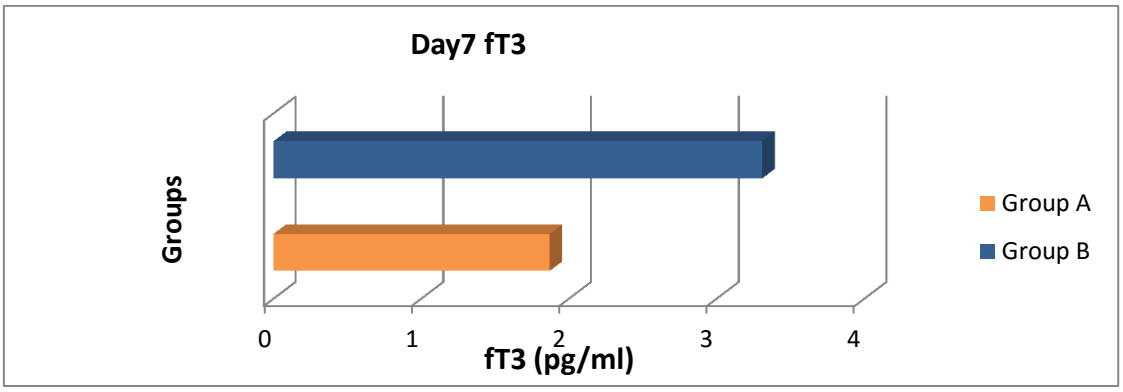


Figure 5.7 fT3 day 7 values

Table 5.8 fT3 day 30 levels.

Day 30	Group A	Group B
Mean (pg/ml)	2.94	3.35
S.D	0.51	0.28
P value	<0.001	

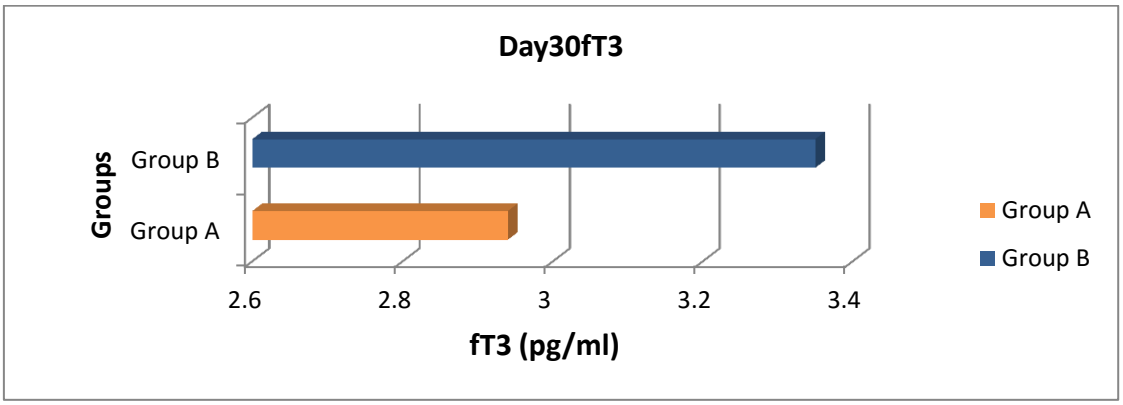


Figure 5.8 fT3 day 30 values.

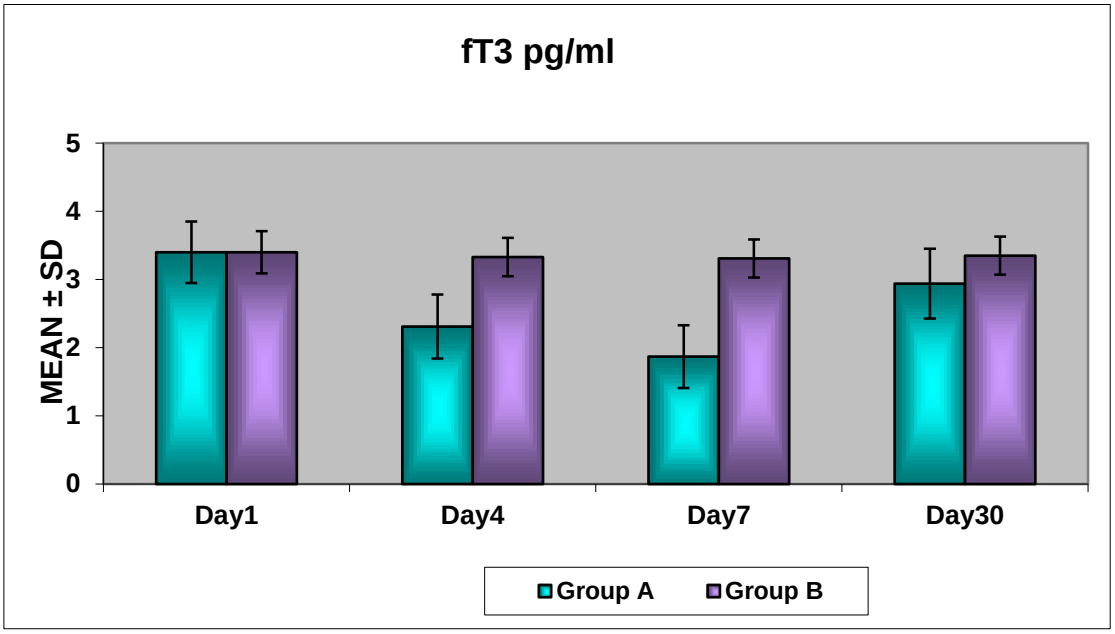


Figure 5.9 ft3 values on day 1 ,4 ,7 ,&30.

Interpretation

fT3 was normal on day 1 in both groups. In group A on day 4&7there was a fall followed by a rise to normal value on day 30. In group B fT3 values were normal throughout the follow up.

Table 5.9 rT3 day 1 values

Day 1	Group A	Group B
Mean (pg/ml)	221.50	220.40
S.D	58.09	40.79
P value	0.913	

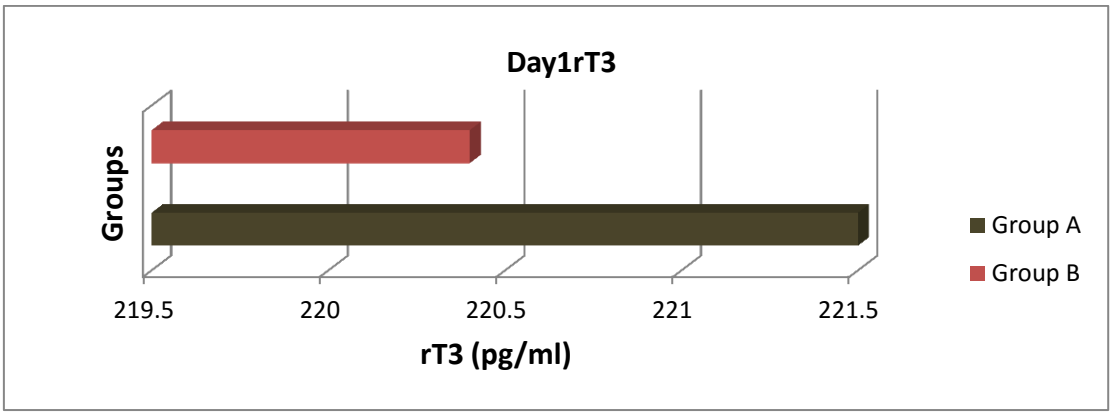


Figure 5.10 day 1 rt3 values

Table 5.10 rT3 day 4 values

Day 4	Group A	Group B
Mean	340.76	230.80
S.D	58.09	41.54
P value	<0.001	

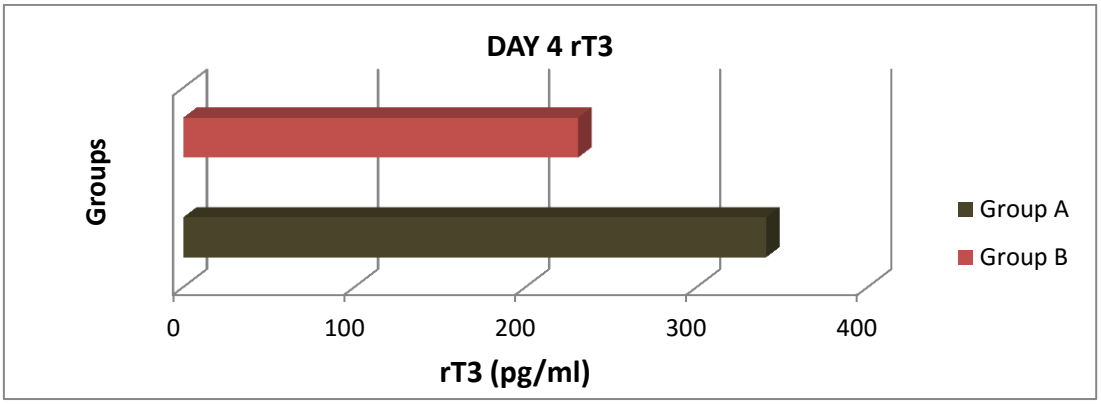


Figure 5.11 rT3 day 4 values

Table 5.11 rT3 day 7 values

Day 7	Group A	Group B
Mean (pg/ml)	393.06	221.10
S.D	29.89	50.54
P value	<0.001	

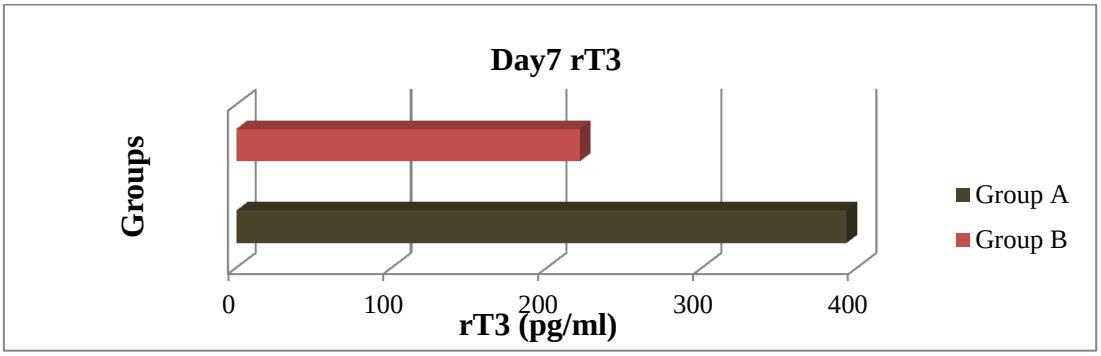


Figure 5.12 rT3 values day 7

Table 5.12 rT3day 30 values

Day 30	Group A	Group B
Mean	231.27	222.40
S.D	59.90	40.47
P value	> 0.05	

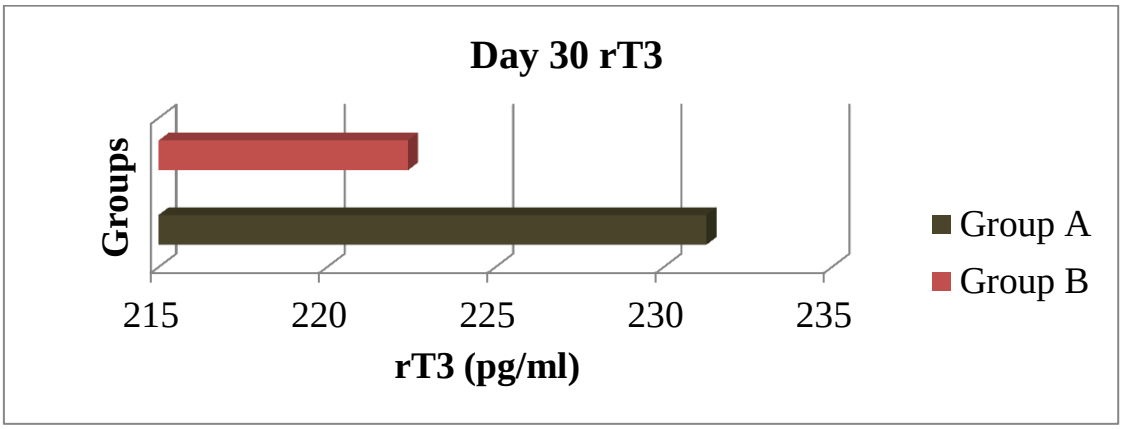


Figure 5.13 rT3 day 30 values

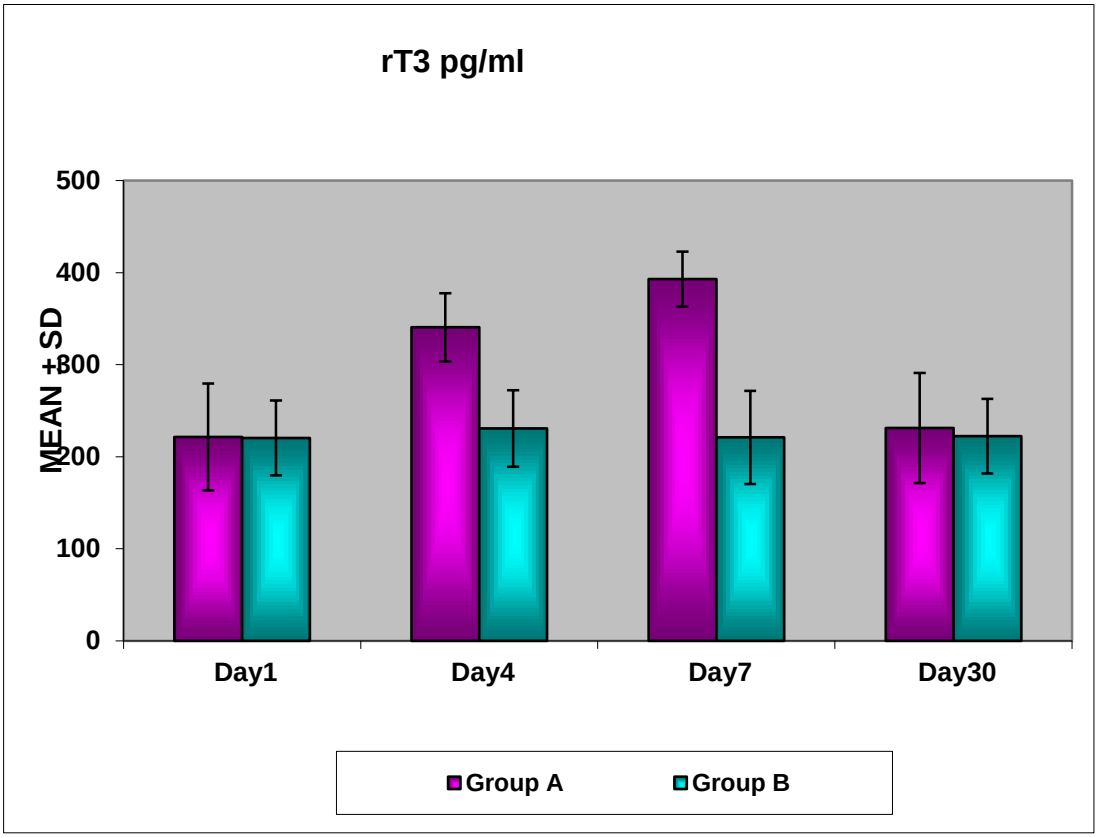


Figure 5.14 rT3 values on day 1, 4, 7, &30

Interpretation

rT3 was normal on day 1 in both groups. In group A on day 4&7there was a rise followed by a fall to normal value on day 30. In group B rT3 values were normal throughout the follow up.

Table 5.13 Distribution of MI in both groups

Type of MI	Group A N(%)	GroupB N(%)	Total N(%)	P value
AWMI	30(60%)	13(26%)	43(43%)	<0.05
IPWMI	11(22%)	9(18%)	20(20%)	>0.05
LWMI	3(6%)	14(28%)	17(17%)	<0.05
NSTEMI	10(20%)	15(30%)	25(25%)	>0.05

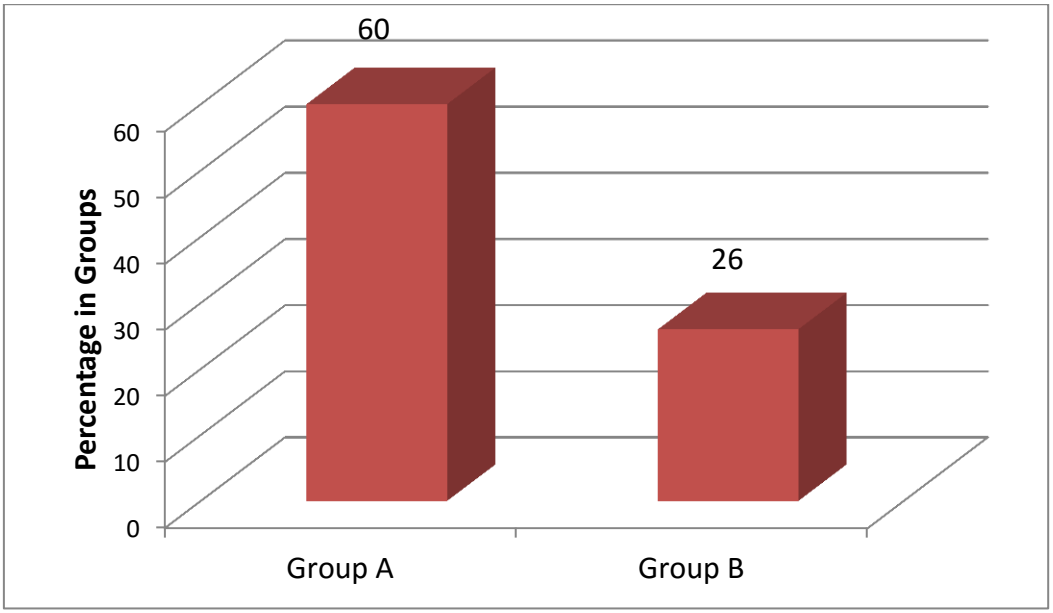


Figure 5.15 Distribution of AWMI in two groups

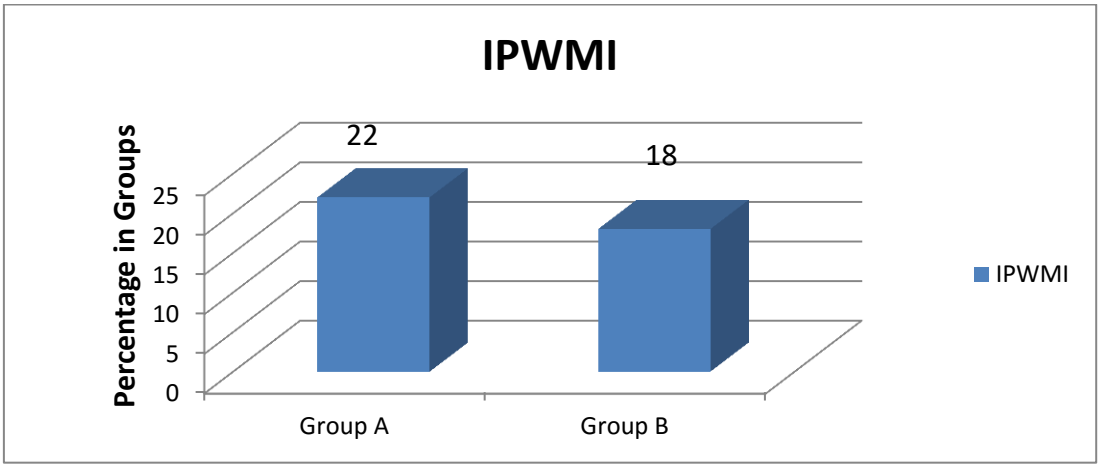


Figure 5.16 Distribution of IPWMI in two groups

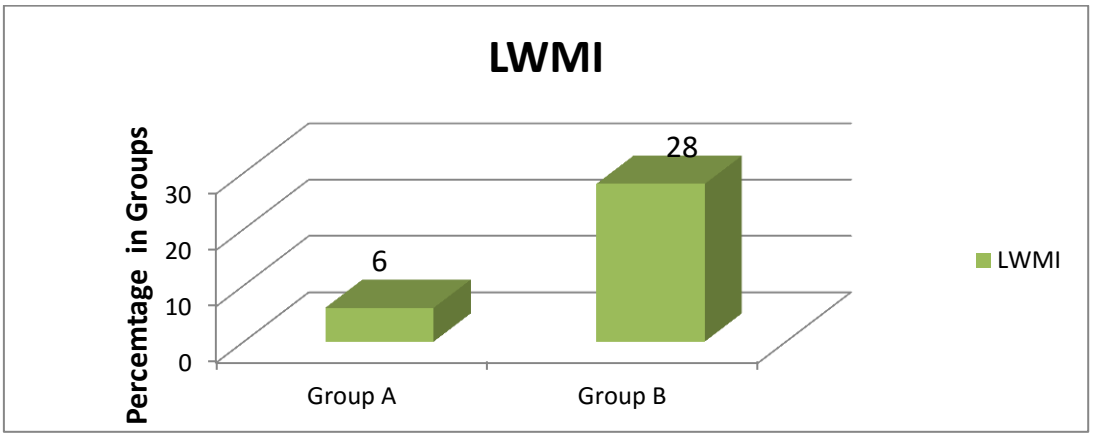


Figure 5.17 Distribution of LWMI in two groups

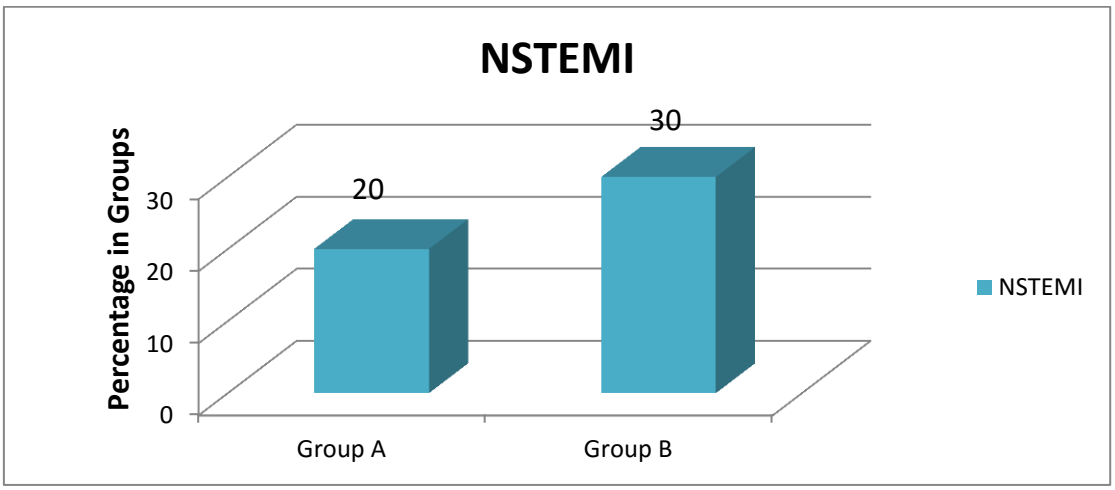


Figure 5.18 Distribution of NSTEMI in two groups

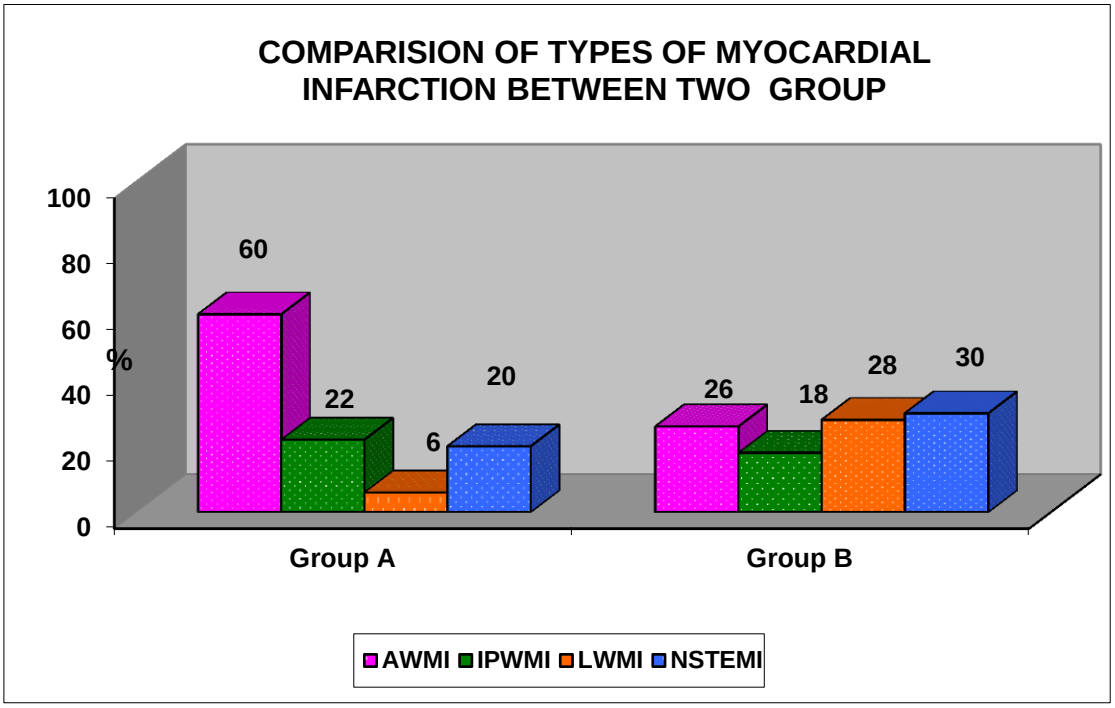


Figure 5.19 Comparison of all types of MI between two groups

Interpretation

Increased incidence of AWMI was seen in group A. Increased incidence of LWMI was seen in group B. INFEROPOSTERIOR, NSTEMI are equally distributed in both the groups. Sick euthyroid was more associated with AWMI.

Table 5.14 EF at admission& follow up between two groups:

EF		<30% N(%)	31-40% N(%)	41-50% N(%)	>50% N(%)	Mean	S.D	P value
Adm	GroupA	3(6%)	38(76%)	9(18%)	0(0%)	36.84	4.40	<0.001
	GroupB	0(0%)	3(6%)	29(58%)	18(36%)	49.02	5.19	
1stt month	GroupA	9(18%)	18(37%)	21(43%)	0(0%)	37.40	6.21	<0.001
	GroupB	0(0%)	2(4%)	23(46%)	25(50%)	50.8	4.86	
4th month	GroupA	13(27%)	20(40%)	15(31%)	0(0%)	36.38	6.82	<0.001
	GroupB	0(0%)	3(6%)	19(38%)	28(56%)	50.66	5.43	
7th month	GroupA	13(27%)	21(44%)	13(27%)	0(0%)	36.15	6.83	<0.001
	GroupB	0(0%)	4(8%)	18(36%)	28(56%)	50.64	5.61	
12th month	GroupA	13(27%)	19(42%)	13(28%)	0(0%)	36.62	7.24	<0.001
	GroupB	0(0%)	3(6%)	14(28%)	32(66%)	51.58	4.74	

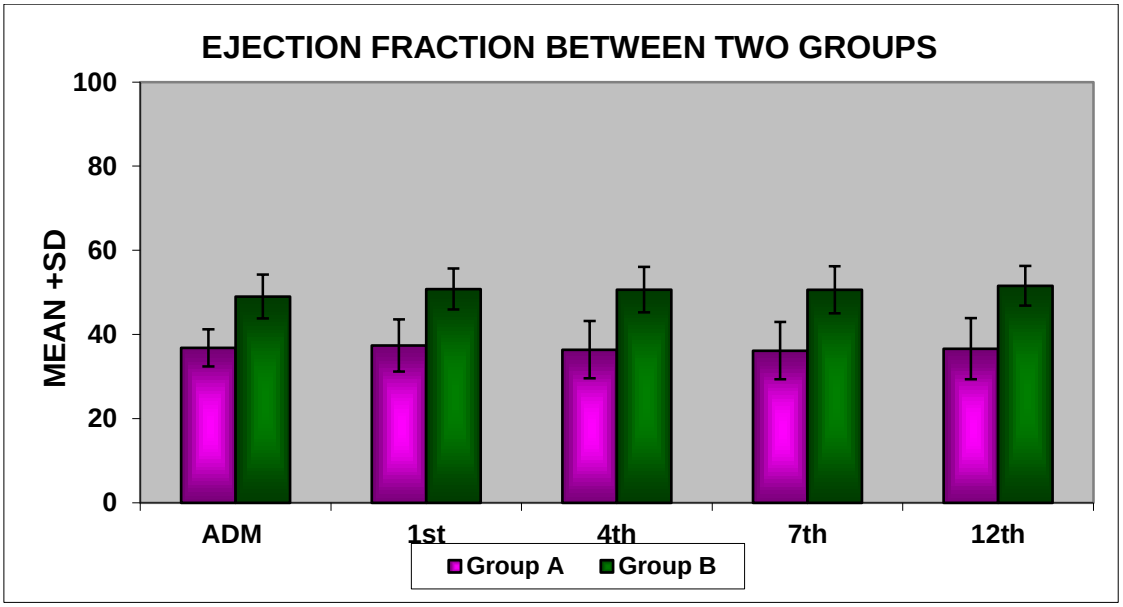


Figure 5.20 Distribution of EF between two groups

Interpretation

Group A patients had decreased EF values at admission and follow up.

Table 5.15 Distribution of ICU stay in two groups

ICU stay	Group A(N=50)	Group B(N=50)
Mean in days	5.5	4.7
S.D	1.19	0.70
P value	<0.001	

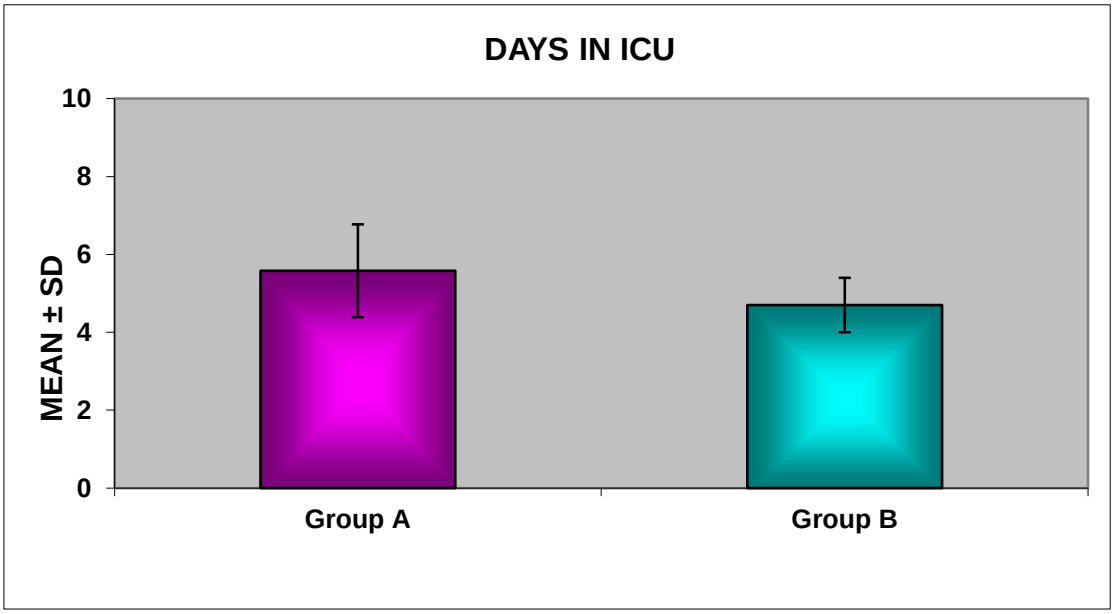


Figure 5.21 Distribution of ICU stay in two groups.

Interpretation

Mean stay in group A is 5.5 days. In group B was 4.7 days. P value was <0.001i.e the duration of ICU stay is longer in group A.

Table 5.16 Distribution of HOSPITAL stay in two groups

HOSPITAL stay	Group A(N=50)	Group B(N=50)
Mean in days	6.9	5.8
S.D	1.09	0.72
P value	<0.001	

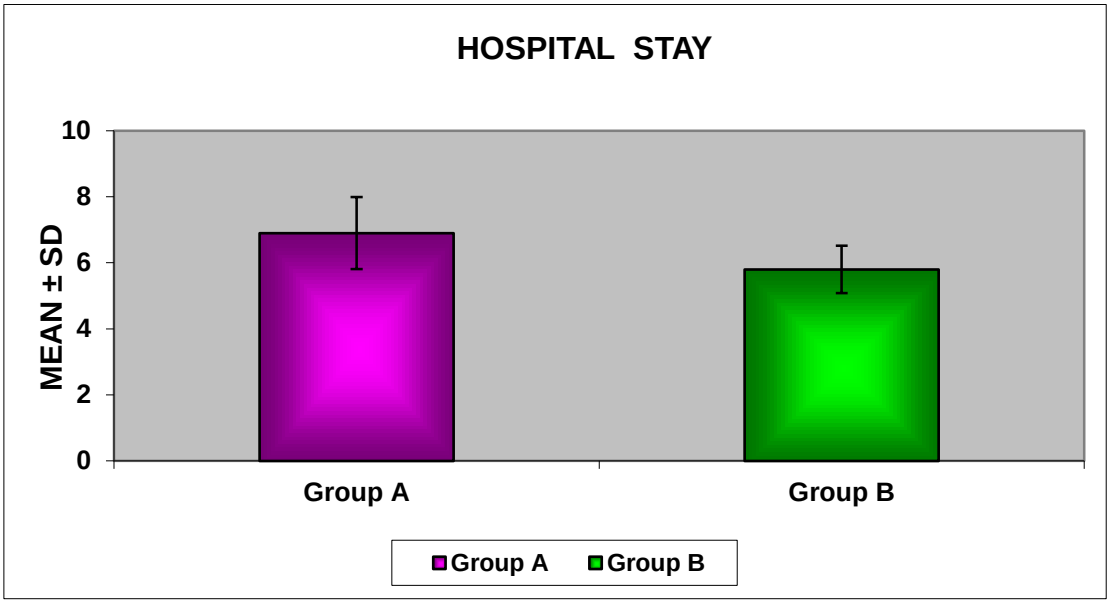


Figure 5.22 Distribution of hospital stay in two groups

Interpretation

Mean stay in group A was 6.9 days. In group B was 5.8 days. P value was <0.001 i.e the duration of HOSPITAL stay is longer in group A.

Table 5.17 Comparison of management between two groups.

Management stratergy	Group A N%	Group B N%	Total N%
CABG	23(48%)	9(18%)	32(33%)
PCI	13(27%)	25(50%)	38(39%)
MEDICAL	12(25%)	16(32%)	28(28%)

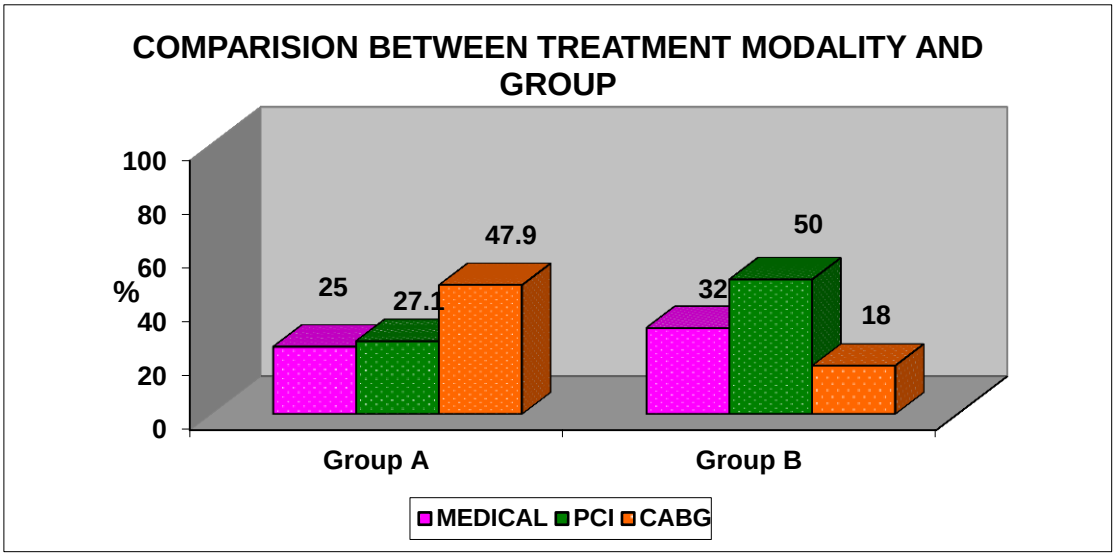


Figure 5.23 Comparison of management between two groups

Interpretation

1. Patients requiring CABG was 48% in group A. In group B it was 18%.

2. Patients requiring PCI was 27% in group A. In group B it was 50%.

3. Patients on medical mangemenet was 25% in group A & 32% in group B.

   Group A patients had more severe disease.

Table 5.18 Distribution of readmission between two groups

Number of times readmitted	Group A N(%)	GroupB N(%)	Total N(%)
1	11(33%)	6(46%)	17(37%)
2	13(40%)	6(46%)	19(41%)
3	5(15%)	1(8%)	6(13%)
≥4	4(12%)	0(0%)	4(9%)

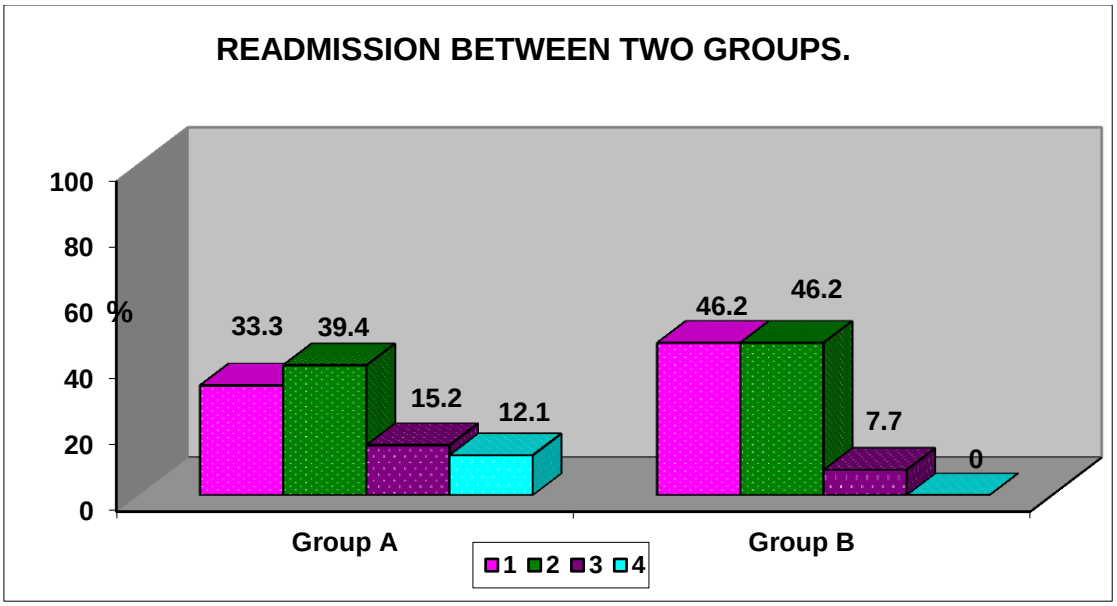


Figure 5.24 Distribution of readmission between two groups

Interpretation

Group A patients needed more re admission than group B with a P value was 0.477

Table 5.19 Distribution of mortality between two groups.

Mortality	Group A N%	Group B N%	Total N%
Immediate	2(40%)	0(0%)	2(33%)
7^{th} month	1(20%)	0(0%)	1(17%)
12^{th} month	2(40%)	1(100%)	3(50%)

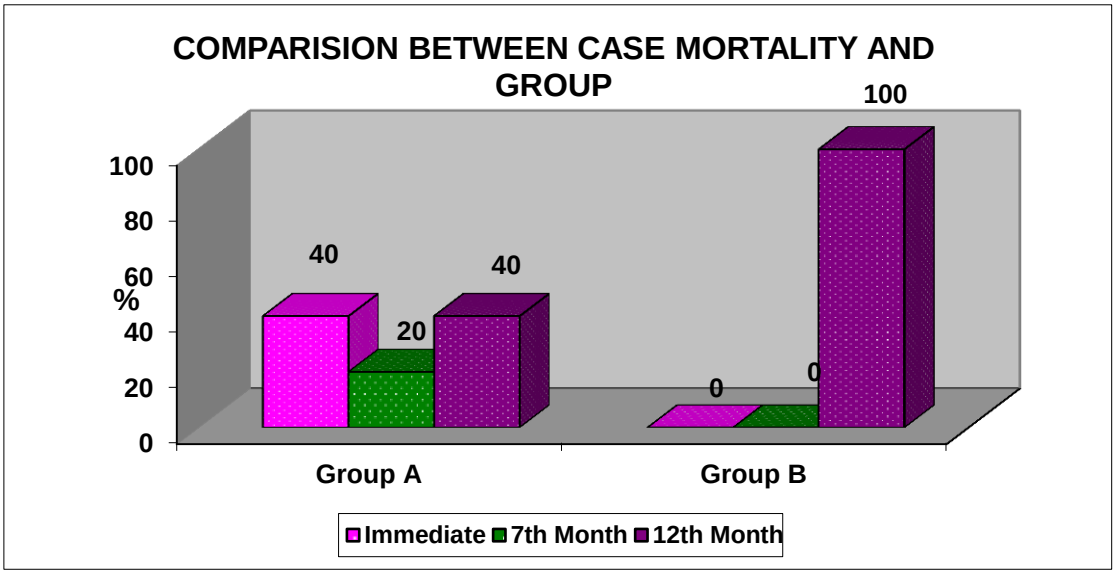


Figure 5.25 Distribution of mortality between two groups

Interpretation

Mortality was more in group A with a P value was 0.549.

DISCUSSION

DISCUSSION

Myocardial infarction was one of the most common critical care emergencies with significant morbidity and mortality. The overall mortality in hospitals was about 6% with a one year mortality of about 10%. The Mortality rate increases fourfold in patients above 75 years of age.

Thyroid hormones were significantly associated with various cardiac illnesses. Coronary Artery Disease (CAD) was also influenced by thyroid dysfunction. Both hypothyroidism and hyperthyroidism were individual risk factors for CAD. Many other risk factors associated with CAD like Hypertension, Diabetes, Dyslipidemia and Atherosclerosis had thyroid dysfunction as an etiology.

The SICK EUTHYROID syndrome has been defined as a state of low fT3 with elevated rT3 and normal T4, TSH levels in the absence of any thyroid or pituitary dysfunction.

Cardiac conditions associated with sick euthyroid include myocardial infarction and chronic heart failure.

In an energy conserving state like myocardial infarction, these low fT3 effects on heart were initially considered as an adaptive mechanism to decrease the cardiac workload.

But various studies had now shown that this condition was rather harmful than having beneficial effects and hence had a significant influence on the short term and long term cardiac events in patients with MI.

In our study 100 patients who satisfied the diagnostic criteria for myocardial infarction were enrolled with informed consent. TSH, fT3, fT4, and rT3 were measured on day1, 4, 7 and 30. Normal reference ranges in our hospital for fT3 is 2.4-4.2 (pg/ml), rT3 is 110-320 (pg/ml), TSH 0.3-4.68 (mIU/L), fT4 0.78-2.19 (ng/ml) respectively.

Based on fT3 &rT3 patients were classified in to two groups:

(1) Group A patients with low fT3 & increased rT3

(2) Group B patients with normal fT3&rT3.

Various morbidity indicators like Electrocardiographic changes, Echocardiography, modes of management, readmission and mortality were compared between the two groups. The role of fT3 and its associated changes in rT3 in predicting the short term & long term mortality and morbidity was studied.

1. AGE DISTRIBUTION

Mean age in group A was 55.14 years and 52.60 years in group B. P value was more than 0.05 with insignificant statistical association between the two groups. Hence the age was equally distributed between the groups.

2. SEX DISTRIBUTION

In our study males constituted 64% and females were 36%. The ratio of male to female was 1.8:1 which was similar to an Indian study conducted by shilpa deoke et al at Nagpur which had a ratio of 2:1. P value was more than 0.05 signifying equal distribution of sex between the two groups.

3. THYROID STIMULATING HORMONE (TSH)

In this study TSH levels were measured on day1, 4, 7 and 30 respectively. The levels were compared between Group A and Group B. The p value was more than 0.05 with an insignificant statistical association.

Deoke et al conducted a study which included 72 patients of Myocardial infarction and measured TSH on days 1 and 7. They reported

that there was no significant statistical difference in TSH levels in patients with sick euthyroid.

4. FREE T4 LEVELS

In our study fT4 was measured on four occasions on day1, 4, 7&30 respectively. Values were compared and it showed an insignificant statistical correlation between the two groups as p value was more than 0.05. The mean fT4 levels were equal between the two groups.

Pimenta et al prospectively studied fT4 levels on days 1, 4 and 7. They also observed that there were no changes in fT4 levels in sick euthyroid patients.

5. FREE T3 LEVELS

In our study the fT3 was measured on day1, 4, 7 and 30 respectively.

In Group A the mean fT3 on day 1 was 3.4pg/ml and there was a fall in fT3 to 2.3 &1.9 pg/ml on day 4 and 7 respectively. The lowest mean value of fT3 was achieved on day7 after that there was a rise in fT3 to 2.9pg/ml on day 30. In group B there was no fall in ft3 level and the mean values were 3.4,3.3, 3.3,&3.3pg/ml on day 1,4,7,&30 respectively.

INFERENCE

Highly significant statistical difference with p value of 0.001 was observed on day 4, 7 and 30. Ioannis Lymvaios et al studied the free t3 levels in myocardial infarction patients and observed a normal baseline level on fT3 on day 1 followed by a fall on day 7 and a slow rise in 6 months which was similar to our study.

6. REVERESE T3 LEVELS

In our study the rt3 was measured on day1, 4, 7 &30 respectively.

In group A the mean rT3 on day 1 was 221.50 (pg/ml) and there was a rise in rt3 level to 340.76 and 393.06 (pg/ml) on day 4 &7 respectively. The highest mean value was achieved on day7, following which there was a fall in rT3 on day 30 to 231.2 (pg/ml).

In group B there was no fall in rT3 level and the mean values were 220.4,230.8,221.1,222.4 (pg/ml) on day 1, 4, 7, &30 respectively.

INFERENCE

High statistically significant difference with p value of <0.001 was found on day 4 and 7.

7. ECG CHANGES

In our study STEMI patients were categorized into anterior, inferoposterior, or lateral wall involvement based on ECG changes and compared between 2 groups. ECG changes in NSTEMI patients were also compared.

In our study the anterior wall involvement was more common with 30 patients in Group A compared to 13 patients in Group B. The p value was significant<.001.

Inferior wall involvement in Group A was 11 compared to 9 patients in Group B. There was no statistical difference between the two groups with a p value of than 0.05. Thus it had an equal distribution between the two groups.

In Group A number of patients with lateral wall involvement was 3 compared to 13 patients in Group B. There was a statistical difference between the two groups with a p value of 0.003.

NSTEMI accounts for 10 patients in group A and 15 patients in group B. There was no statistical difference between the two groups.

INFERENCE

Patients with sick euthyroid had an increased association with AWMI & increased morbidity.

Deoke et al conducted a study on sick euthyroid and myocardial infarction. They concluded that anterior wall involvement was most common among patients with low fT3.

8. ECHOCARDIOGRAM

The severity of MI can be assessed by Echocardiogram by calculating EF values. In our study it was done at admission and on days 1,4,7 and 12^{th} month between the two groups**.**

EF % OF GROUP A & GROUP B AT ADMISSION

EF (%)	Group A (N%)	Group B (N%)
< 30	3 (6%)	0
31-40	38 (76%)	3 (6%)
41-50	9 (18%)	29 (58%)
> 50	0 (%)	18 (36%)

- Group A had more no.of patients with moderate to severe LV dysfunction at admission.

- Group B had more number of patients with mild LV dysfunction and normal LV function at admission.

EF % OF GROUP A & GROUP B AT THE END OF FOLLOW UP

EF (%)	Group A (N%)	Group B (N%)
< 30	13 (27%)	0
31-40	19 (42%)	3 (6%)
41-50	13 (28%)	14 (28%)
> 50	0 (%)	32 (66%)

- Group A had more no.of patients with moderate to severe LV dysfunction at the end of follow up.
- Group B had more no.of patients with good LV function at the end of follow up.

INFERENCE

1) Group A patients had severe to worsening LV function at admission and during the follow up.

2) Group B patients had milder forms of LV dysfunction which improved on follow up.

3) Hence it can be concluded that Group A patients with low fT3 & raised rT3 consistently show poor long term prognosis in our study.

Loannis Lymvaios et al conducted a study in myocardial infarction and grouped them in to two with an EF <50 % taken as cut off point. They observed that patients with ejection fraction of less than 50% significantly correlated with low fT3 levels at admission & follow up. And they concluded that low fT3 has an effect on delaying the recovery among cardiac patients.

ShilpaDeoke et al conducted a study with an EF< 40% as cut off point and they observed that there were significantly increased number of patients with low fT3 and reduced ejection fraction. Further they concluded that MI patients with low fT3 had a poor LV function.

10. DURATION OF ICU STAY

The mean number of stay at ICU was 5.5 days among Group A as compared to Group B where it was 4.7days. And it showed a statically significant with a p value <0.001.

INFERENCE

There was a delay in the short term recovery of patients in sick euthyroid group.

11. DURATION OF HOSPITAL STAY

The mean duration of hospital stay in group A was 6.9 days but in Group B it was only about 5.8 days with a significant p value.

INFERENCE

It can be concluded that there was a definite delay in the short term recovery of patients with sick euthyroid.

12. COMPARISON OF MANAGEMENT STRATERGIES LIKE PCI, CABG, CONSERVATIVE MANAGEMENT BETWEEN THE TWO GROUPS:

	GROUP A (%)	GROUP B (%)
CABG	48%	18%
PCI	27%	50%
MEDICAL	25%	32%

INFERENCE

(1) There was a statistically significant difference of 0.05 in the management strategies between the two groups.

(2) Patients with sick euthyroid had an increased morbidity as there were increased requirement of CABG when compared with PCI.

(3) 25%of patients needing medical management in group A were inoperable due to factors like severe LV dysfunction& scarred myocardium.

13. READMISSION

In our study the number of readmissions with MACE (major adverse cardiac events) was 33 in Group A compared to 13 in Group B. There was no statistical difference between the two groups and the p value was 0.477 in spite of increased number of readmissions in Group A.

Kazım Serhan Özcan et al conducted a study on MACE events in patients with sick euthyroid and they reported a statistically significant increase in MACE events among them. In their study about 457 patients were included and were followed up for 14 months.

Hence to show a statistically significant result, the sample size and the duration of follow up needs to be increased.

14. MORTALITY

In our study the total mortality among patients with sick euthyroid was 10% but in Group B with normal fT3 and rT3 it was only about 2% with a ratio of 5:1. There was no statistical difference between the two groups as the p value was 0.549.

Kazım Serhan Özcan et al conducted a study among 457 myocardial patients. They observed during follow up, sick euthyroid patients when compared with control group had an increased mortality in the ratio of 5:1 with statistical significance.

Friberg et al conducted a study measuring rT3 levels of 331 patients with myocardial infarction. And they showed that there was an increased one year mortality among patients with increased rT3 levels.

Lazzeri et al conducted a study among 641 patients with STEMI and observed that the in-hospital mortality was high in patients with sick euthyroid patients.

In another study conducted by Molinaro et al, the observed cardiac mortality was very high in patients with sick eutyhroid. They conducted their study in 1026 patients with acute cardiac diseases and were followed for 30 months.

Our study also showed increased mortality in group A.

Here also it can be concluded that to show a significant statistical difference, it was mandatory to increase the sample size and duration of follow up.

SUMMARY

Myocardial infarction is a common medical emergency needing critical care. Its incidence across the globe is on the rise. The in hospital & 1 year mortality is about 6%&10% respectively. So the need to identify markers that can predict poor outcomes in myocardial infarction is on the rise. The association between thyroid & cardiovascular diseases are well studied. Sick euthyroid syndrome is a hypothyroid state in the absence of thyroid illness. This study was conducted as to whether sick euthyoid syndrome characterised by low fT3&elevated rT3 can predict poor prognosis in myocardial infarction patients.

Our study confirmed that myocardial infarction had an increased incidence in males in age group 40 -60 years. AWMI had more association with sick euthyroid syndrome.

Mean duration of ICU stay in sick euthyroid group was (5.5 ± 1.1) days, compared to (4.7 ±0.7) in control group . Mean duration of HOSPITAL stay in sick euthyroid group was (6.9±1.09) days, compared to (5.8 ± 0.7) in control group. Both indicators had statistical significance. P value was < 0.001(significant).

Mean ejection fraction in echocardiography was 36% in sick euthyroid group when compared to 49% in control group at admission. During follow up EF values were 36% & 51% respectively. P value was significant (<0.01). Sick thyroid patients had depressed EF throughout the study.

48% of patients needed invasive management like CABG compared to 18% in control group. Hence sick euthyroid patients needed more invasive management stratergies.

Number of readmission & mortality was more in sick euthyroid group.

CONCLUSION

CONCLUSION

- Incidence of MI was more in males in the age group of 40-60.
- Decrease in fT3 & increase in rT3 was observed after day1 of MI with peak values on day7 in sick euthyroid patients.
- Short term morbidity indicators such as duration of ICU AND HOSPITAL stay was prolonged in MI patients with sick euthyroid syndrome.
- Long term morbidity indicators such as LV dysfunction & delayed recovery of LV function was more in MI patients with sick euthyroid syndrome.
- Invasive &early interventional management strategies were needed in sick euthyroid patients because of their delay in recovery.
- AWMI was more common in sick euthyroid patients with poor prognosis.
- Hence identifying sick euthyroid syndrome in MI patients is important in predicting their short &long term morbidity.

LIMITATIONS

LIMITATIONS

- Inadequate sample size
- Needs increased duration of follow up.
- Unstable angina patients were not included and their influence on the outcome is unknown.
- Other co morbid factors like hypertension,diabetes, dyslipidemia which can influence the outcome in a CAD patient needs to be evaluated further.

FUTURE PROSPECTIVES

FUTURE PROSPECTIVES

- A simple thyroid function test is very helpful to predict the prognosis of myo cardial infarction patients.

- This is more useful when taken to the community level. And it is most useful in extremely rural (unapproachable rural area) areas where other investigative tools like echocardiogram are not available, where the clinician can predict the outcome of myocardial infarction patients with the simple thyroid function test.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Longo, D. L., Fauci, A. S., Kasper, D. L., Hauser, S. L., & Loscalzo, J. (2016). *Harrisons manual of medicine, 19th edition (Kasper, Harrison's manual of medicine)* (19th ed.). New York: McGraw-Hill Professional.

2. Zipes, D. P., Libby, P., Braunwald, E., & Peter, L. (2015). Braunwald's heart disease: A textbook of cardiovascular medicine (10th ed.). Philadelphia, PA: Saunders (W.B.) Co.

3. Abdulaziz qari F. Thyroid Hormone Profile in Patients With Acute Coronary Syndrome. Iran Red Crescent Med J. 2015;17(7):e26919.

4. Özcan KS, Osmonov D, Toprak E, et al. Sick euthyroid syndrome is associated with poor prognosis in patients with ST segment elevation myocardial infarction undergoing primary percutaneous intervention. Cardiol J. 2014;21(3):238-44.

5. Adawiyah J, Norasyikin AW, Mat NH, Shamsul AS, Azmi KN. The non-thyroidal illness syndrome in acute coronary syndrome is associated with increased cardiac morbidity and mortality. Heart Asia. 2010;2(1):11-4.

6. Coceani M, Iervasi G, Pingitore A, Carpeggiani C, L'abbate A. Thyroid hormone and coronary artery disease: from clinical correlations to prognostic implications. Clin Cardiol. 2009;32(7):380-5.

7. Pimentel RC, Cardoso GP, Escosteguy CC, Abreu LM. Thyroid hormone profile in acute coronary syndromes. Arq Bras Cardiol. 2006;87(6):688-94.

8. Pavlou HN, Kliridis PA, Panagiotopoulos AA, Goritsas CP, Vassilakos PJ. Euthyroid sick syndrome in acute ischemic syndromes. Angiology. 2002;53(6):699-707.

9. Friberg L, Drvota V, Bjelak AH, Eggertsen G, Ahnve S. Association between increased levels of reverse triiodothyronine and mortality after acute myocardial infarction. Am J Med. 2001;111(9):699-703.

10. Lazzeri C, Sori A, Picariello C, Chiostri M, Gensini GF, Valente S. Nonthyroidal illness syndrome in ST-elevation myocardial infarction treated with mechanical revascularization. Int J Cardiol. 2012;158(1):103-4.

11. Jankauskienė E, Orda P, Rumbinaitė E, et al. Left ventricular function by speckle-tracking echocardiography in patients with low-T3 syndrome and acute myocardial infarction. Medicina (Kaunas). 2015;51(4):209-16.

12. Zhang B, Peng W, Wang C, Li W, Xu Y. A low fT3 level as a prognostic marker in patients with acute myocardial infarctions. Intern Med. 2012;51(21):3009-15.

13. Lymvaios I, Mourouzis I, Cokkinos DV, Dimopoulos MA, Toumanidis ST, Pantos C. Thyroid hormone and recovery of cardiac function in patients with acute myocardial infarction: a strong association?. Eur J Endocrinol. 2011;165(1):107-14.

14. Yazici S, Kiris T, Ceylan US, et al. Relation of Low T3 to One-Year Mortality in Non-ST-Elevation Acute Coronary Syndrome Patients. J Clin Lab Anal. 2016;

15. Daswani R, Jayaprakash B, Shetty R, Rau NR. Association of Thyroid Function with Severity of Coronary Artery Disease in Euthyroid Patients. J Clin Diagn Res. 2015;9(6):OC10-3.

16. Wang WY, Tang YD, Yang M, et al. Free triiodothyronine level indicates the degree of myocardial injury in patients with acute ST-elevation myocardial infarction. Chin Med J. 2013;126(20):3926-9.

17. Lee S, Farwell AP. Euthyroid Sick Syndrome. Compr Physiol. 2016;6(2):1071-80.

18. Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of thyroid hormone on cardiac function: the relative importance of heart rate, loading conditions, and myocardial contractility in the regulation of cardiac performance in human hyperthyroidism. J Clin Endocrinol Metab. 2002;87(3):968-74.

19. Saurabh Potdar, Hetal Patel et al. Evaluation Of Thyroid Dysfunction In Acute Coronary Syndrome. NJIRM. 2013; 4(5): 65-71.

20. Medha Rajappa and S.K. Sen etal. Evaluation of thyroid hormone status after acute myocardial infarction in South Indians. Vol. 16, No. 1 (2005-01 - 2005-03).

21. Shilpa Deoke , Ujwala Walv etal. Sick euthyroid syndrome in acute myocardial infarction and its correlation with left ventricular function.. |Vol3| Issue1| 2014.

22. Iervasi G, Landi P, Raciti M, et al. Low-T3 syndrome: a strong prognostic predictor of death in patients with heart disease. Circulation 107: 708-713, 2003.

23. Ascheim DD, Hryniewicz K. Thyroid hormone metabolism in patients with congestive heart failure: the low triiodothyronine state. Thyroid12 : 511-515, 2002.

24. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med344 : 501-509, 2001.

25. Pingitore A, Iervasi G, Barison A, et al. Early activation of an altered thyroid hormone profile in asymptomatic or mildly symptomatic idiopathic left ventricular dysfunction. J Card Fail 12: 520-526, 2006.

26. Pantos C, Mourouzis I, Cokkinos DV. Thyroid hormone as a therapeutic option for treating ischaemic heart disease: from early reperfusion to late remodelling. Vascul Pharmacol 52: 157-165, 2010.

27. Bermudez F, Surks MI & Oppenheimer JH. High incidence of decreased serum triiodothyronine concentration in patientswith

nonthyroidal disease. Journal of Clinical Endocrinology and Metabolism1975 27–40. (doi:10.1210/jcem-41-1-27).

28. Eber B, Schumacher M, Langsteger W, Zweiker R, Fruhwald FM, Pokan R, Gasser R, Eber O & Klein W. Changes in thyroid hormone parameters after acute myocardial infarction. Cardiology1995 152–156. (Doi:10.1159/000176862).

29. Franklyn JA, Gammage MD, Ramsden DB & Sheppard MC. Thyroid status in patients after acute myocardial infarction.Clinical Science1984 585–590.

30. Friberg L, Werner S, Eggertsen G & Ahnve S. Rapid down-regulation of thyroid hormones in acute myocardial infarction: is it cardioprotective in patients with angina?Archives of Internal Medicine 20021388–1394. (doi:10.1001/archinte.162.121388).

31. Pol CJ, Muller A, Zuidwijk MJ, Van Deel ED, Kaptein E, Saba A,Marchini M, Zucchi R, Visser TJ, Paulus WJ, Duncker DJ &Simonides WS. Left-ventricular remodeling after myocardial infarction is associated with a cardiomyocyte-specific hypothyroid condition.Endocrinology2011 152669–679. (doi:10.1210/en.2010-0431).

32. Forini F, Lionetti V, Ardehali H, Pucci A, Cecchetti F, Ghanefar M, Nicolini G, Ichikawa Y, Nannipieri M, Recchia FA & Iervasi G. Early long-termT3 replacement rescues mitochondria andprevents ischemic cardiac remodeling in rats.Journal of Cellularand Molecular Medicine 2010 15514–524. (doi:10.1111/j.1582-4934.2010.01014.x).

33. Pantos C, Mourouzis I, Markakis K, Tsagoulis N, Panagiotou M & Cokkinos DV. Long term thyroid hormone administration reshapes left ventricular chamber and improves cardiac function after myocardial infarction in rats. Basic Research in Cardiology 2008103308–318. (doi:10.1007/s00395-008-0697-0).

34. J lein I, Ojamaa K. Thyroid hormone and the cardio vascular system. NEnglJMed. 2001;344: 501–509.

35. Lervasi G, Pingitore A, Landi P, et al. Low-T3 syndrome: a strong prognostic predictor of death in patients with heart disease. Circulation. 2003;107:708–713.

36. Eber B, Schumacher M, Langsteger W, Zweiker R, Fruhwald FM, Pokan R, et al. Changes in thyroid hormone parameters after acute myocardial infarction. Cardiology 1995; 86:152-56.

37. Holland FW, Brown PS, Weintraub BD, Clark RE. Cardiopulmonary bypass and thyroid function: a “euthyroid sick syndrome”. Ann Thorac Surg 1991; 52(1) : 46-50.

38. Duntas LH, Nguyen TT, Keck FS, Nelson DK, DiStefano JJ. Changes in metabolism of TRH in euthyroid sick syndrome. European Journal of Endocrinology 1999;141: 337-341.

39. Hamilton MA, Stevenson LW, Luu M, Walden JA.Altered thyroid hormone metabolism in advanced heart failure. Journal of the American College of Cardiology 1990; 16: 91–95.

40. Wiersinga WM, Lie KI, Touber JL.Thyroid hormones in acute myocardial infarction. Clin Endocrinol. 1981; 14:367-374.

41. GG Gensini. A more meaningful scoring system for determining the severity of coronary heart disease. The American journal of cardiology. 1983;51(3):606.

42. A Peters, M Ehlers, B Blank, D Exler, C Falk, T Kohlmann, et al. Excess triiodothyronine as a risk factor of coronary events. Arch Intern Med. 2000;160(13):1993–99.

43. J Auer, R Berent, T Weber, E Lassnig, B Eber. Thyroid function is associated with presence and severity of coronary atherosclerosis. Clin Cardiol. 2003;26(12):569–73.

44. S Razvi, L Ingoe, G Keeka, C Oates, C McMillan, JU Weaver. The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. J Clin Endocrinol Metab. 2007;92(5):1715–23.

45. WILSON PW, D'AGOSTINO RB, LEVY D, et al: Prediction of coronary heart disease using risk factor categories. Circulation 97:1837-1847, 1998.

46. Docter R, Krenning EP, deJong M, et al. The sick euthyroid syndrome: chranges in thyroid hormone serum parameters and hormone metabolism. Clin Endocrinol 1993; 39: 499-518.

47. Hamilton M, Stevenson L, Luu M. Altered thyroid hormone metabolism in advanced heart failure. J Am Coll Cardiol 1990; 16: 91-95.

48. Wartofsky L and Burman K. Alterations in thyroid function in patients with systemic illness: the “Euthyroid sick syndrome’. Endocrine Reviews 1982; 3: 164-217.

49. Boelen A, Plavoet-Ter Schiphorst MC and Wiersinga WM. Association between serum interleukin-6 and serum 3,5,3’ – tricodothyronine in nonthyroidal illness. J Clin Endocrinol Me-tab 1993; 77: 1695-1699.

50 Klein I. Thyroid hormone and the cardiovascular system. Am J Med 1990; 88: 626-630.

51. Klein I. Thyroid hormone and the cardiovascular system. Am J Med 1990; 88: 626-630.

52. Dillman WH. Biochemical basis of thyroid hormone action in the heart. Am J Med 1990; 88: 626-630.

53. Krause SM, Jacobus WE, Becker LC. Alterations in cardiac sarcoplasmic reticulum calcium transport in the post ischemic “stunned” myocardium. Cir Res 1989; 65: 526-530.

54. Gonarkar SB, Dhande, PP Medication adherence and its determinants in myocardial infarction patients: An. Indian Scenario. J.Clin. Prev Cardiol 2016; 5:2-8.

ANNEXURES

PROFORMA

Name : Address :

Age : Socio economic status :

Sex : Education :

IP Number :

Detailed history:

Past History :diabetic/hypertension/smoking/alchoholic.

Vital signs :pulse/blood pressure /oxygen saturation.

General examination :

C V S :

R S :

Abdomen :

CNS:

Investigation :

a.Serial ecg

b Enzymes:TROP-I,CPK,CK-MB.

c. Thyroid Funtion Test : fT3, T4, TSH, rT3

d. Echocardiography

e. FBS/PPBS.

f . Fasting lipid profile

g .Renal Funtion Test

h. Liver Funtion Test.

i. CBC

Date of Admission :

Date of Discharge :

Duration of ICU/hospital stay :

Number of days/ years of survival in case of mortality:

Number of times and duration of Re-admission for the following complications during one year :

a. Arrthymias

b. Post infarct angina

c. post infarct failure.

PATIENT CONSENT FORM

Study title: TO STUDY THE ROLE OF ft3 AND rt3 IN PREDICTING THE MORTALITY AND MORBIDITY IN STEMI AND NSTEMI PATIENTS

Study centre : ESIC Medical College - PGIMSR

Participant name : **Age** :

Sex : **IP No** :

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to clarify all my queries and doubts and they have been answered to my satisfaction.

Investigator explained very well about the procedure and I am made aware of the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is purely voluntary and that I am free to withdraw at anytime without giving any reason.

I have understood that the investigator, regulatory authorities and the ethics committee will have access to my health records both in respect to current study and any further research that may be conducted in relation to it, even if I decide to withdraw from the study. I have understood that my identity will not be revealed in anyway and information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Without any compulsion I am willing to give consent for the participation of myself in this study.

Date:

Place:

Signature of the investigator: Signature / thumb impression of patient

Name of the investigator: Patient name:

INFORMATION TO PARTICIPANTS

Investigator: Dr.G Sakthiram

Study centre: ESIC Medical College - PGIMSR, K.K.Nagar, Chennai

Title: TO STUDY THE ROLE OF ft3 AND rt3 IN PREDICTING THE MORTALITY AND MORBIDITY IN STEMI AND NSTEMI PATIENTS".

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria.

Rights and confidentiality:

The participation in this study is purely voluntary. You have every right not to participate in this study. All the data collected in this regard from you will be kept discretely and your name will not be revealed at any circumstances.

To contact:

If you have any doubts and clarification required you can call the doctor ,

G SAKTHIRAM. at the 9865891214 mobile number at any time.

Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator: _____

Name of the Investigator : _____

ANNEXURES – II

ஒப்புதல் படிவம்

பெயர்: வயது:

இனம்: காப்பீட்டு எண்:

நான் இரத்த மற்றும் இருதய பரிசோதனையின் மூலம் செய்யும் இந்த ஆய்வின் நோக்கத்தை புரிந்து கொண்டேன். மேலும் இந்த ஆய்வினை பற்றி சந்தேகங்களை ஏற்படும் நிலையில் எனது சந்தேகங்களை முழுமையாக விளக்கப் பெறலாம் என்பதையும் அறிந்து கொண்டேன்.

நான் எனது சொந்த விருப்பத்தின் பேரில் இந்த ஆய்விற்கு சம்மதிக்கிறேன். மேலும் எந்த நிலையிலும் நான் இந்த ஆய்விலிருந்து விலகிக் கொள்ளலாம் என்பதையும் அறிந்து கொண்டேன்.

மேலும் இந்த ஆய்விலிருந்து நான் விலகிக்கொண்டாலும் எனது உடல் பரிசோதனைகளின் முடிவுகளை இந்த ஆய்விற்கும் மற்றும் பின்வரும் ஆய்வுகளுக்கும் பயன்படுத்தலாம் என்பதையும் அறிந்து கொண்டேன்.

மேலும் அவசியமின்றி எனது பெயரோ, புகைப்படமோ எந்த நிலையிலும் வெளியிடப்படமாட்டாது என்பதையும் அறிந்து கொண்டேன்.

இவை அனைத்தும் தெரிந்தும் என்னுடைய சொந்த விருப்பத்தின் பேரில் நான் இந்த ஆய்விற்கு சம்மதிக்கிறேன்.

தேதி:

இடம்: கையொப்பம்

MASTER CHART

KEY TO MASTER CHART

1.	ECG	-	Electro Cardiogram
2.	AWMI	-	Anterior Wall Myocardial Infarction
3.	IPWMI	-	Infero Posterior Wall Myocardial Infarction
4.	LWMI	-	Lateral Wall Myocardial Infarction
5.	NSTEMI	-	Non ST Elevation Myocardial Infarction
6.	PCI	-	Percutaneous Coronary Intervention
7.	CABG	-	Coronary Artery Bypass Graft

MASTER CHART (GROUP A)

S.No	Age	Sex	ECG				Echocardiogram(EF) in %months					Free T3 pg / ml				Reverse T3 pg/ml				TSH Miu/l				ft4 in ng/ml				Days in ICU	Hosp stay	Readmission	Treatment modality			case mortality				
			AWMI	IPWMI	LWMI	NSTEMI	AT ADM	1	4	7	12	Day1	Day4	Day7	Day30	Day1	Day4	Day7	Day30	day1	day4	day7	day30	day1	day4	day7	day30				Medical	PCI	CABG	Immediate	1st	4th	7th	12th
1	58	F	y				36	32	30	29	29	4.12	2.45	1.56	3.53	130	357	420	150	3.1	3.12	3.12	3.11	1.4	1.35	1.38	1.35	6	7	3	y								
2	64	M		y			42	41	39	38	35	3.45	2.76	2.15	2.95	225	335	380	210	3.05	3.11	3.1	3.1	1.3	1.29	1.28	1.28	5	7	n			y						
3	60	M	y				38	36	36	35	35	3.75	1.93	1.75	3.52	177	385	410	225	3.19	3.15	3.15	3.11	1.45	1.45	1.45	1.45	4	6	2			y						
4	65	F	y				30	28	27	25	n	3.15	1.53	0.91	2.45	248	301	440	216	3.4	3.65	3.75	3.54	0.9	0.9	0.9	0.9	8	10	4	y								y
5	72	F	y	y			31	27	25	23	22	3.35	0.9	0.85	2.35	240	450	480	205	2.45	2.45	2.45	2.45	1.2	1.2	1.2	1.2	6	7	2	y								
6	55	M	y				39	42	42	42	42	3.42	2.34	2.05	2.75	195	350	390	182	3.75	3.78	3.72	3.7	1.15	1.05	1.1	1.15	4	6	n			y						
7	48	F				y	44	41	41	40	40	4.1	2.75	2.34	3.8	140	320	380	130	1.95	1.95	1.95	1.95	1.45	1.45	1.45	1.45	5	7	1		y						
8	38	M		y			42	41	40	41	40	3.14	2.6	2.25	3	260	355	370	250	1.7	1.73	1.75	1.73	1.92	1.9	1.96	1.94	5	7	1		y						
9	44	F	y				38	40	40	40	40	3.83	2.65	2.2	3.34	150	306	400	190	3.05	3.05	3.05	3.05	1.73	1.75	1.75	1.75	4	6	n			y						
10	60	M	y				33	32	32	32	31	3.1	1.9	1.83	2.85	270	370	415	165	2.96	2.98	2.96	2.96	1.45	1.45	1.45	1.45	7	8	2			y						
11	65	M	y	y			25	n	n	n	n	2.4	0.9	n	n	285	400	n	n	3.75	3.75	n	n	0.95	0.95	n	n	4	4	n				y					
12	50	M	y				37	35	35	35	36	3.5	2.42	2.25	3.04	190	265	425	205	2.83	2.8	2.85	2.83	1.05	1.05	1.05	1.03	5	7	1			y						
13	50	M				y	43	42	41	41	41	3.3	2.15	2.24	2.9	250	375	355	275	2.65	2.65	2.65	2.65	1.23	1.23	1.23	1.23	5	5	n			y						
14	60	F	y				34	30	29	27	26	2.9	1.73	1.17	2.2	280	390	450	325	3.1	3.1	3.1	3.1	1.62	1.64	1.62	1.62	7	8	4			y						
15	70	M	y				32	22	20	24	n	3.76	2.22	1.67	3.14	185	350	415	198	3.12	3.12	3.12	3.12	1.06	1.06	1.06	1.06	8	8	3	y								y
16	40	M		y			39	40	40	39	38	3.1	2.95	2.52	2.76	240	310	360	235	2.94	2.94	2.94	2.94	1.27	1.27	1.3	0.3	5	7	1			y						
17	46	M				y	38	41	40	40	40	4.15	2.8	2.21	3.76	130	300	355	140	2.25	2.21	2.25	2.24	1.94	1.94	1.94	1.94	4	7	2			y						
18	58	F	y				40	44	44	45	45	4.1	2.43	2.3	3.4	140	320	376	190	1.45	1.43	1.45	1.45	1.5	1.55	1.55	1.55	5	7	n			y						
19	69	M	y	y			24	n	n	n	n	2.8	1.7	0.8	n	290	400	450	n	3.35	3.35	3.35	n	1.43	1.43	1.43	n	8	8	n				y					
20	44	M			y		40	45	45	45	46	3.5	2.36	2.18	3.05	215	325	360	270	3.25	3.3	3.25	3.25	1.18	1.18	1.18	1.18	4	6	n		y						
21	60	F	y				34	31	29	28	28	3.1	2.3	1.57	2.26	290	345	405	300	3.65	3.65	3.63	3.62	1.15	1.15	1.15	1.15	6	7	1			y						
22	55	M		y			33	35	35	35	35	3.9	3	2.37	3.18	150	280	350	180	3.21	3.2	3.2	3.2	1.43	1.43	1.43	1.43	4	6	3		y						
23	49	F				y	39	42	41	39	38	4.1	2.87	2.41	3.56	140	280	360	190	2.95	2.9	2.9	2.9	1.36	1.38	1.36	1.36	5	6	n			y						
24	46	M	y				42	49	50	50	48	4.2	2.6	2.23	3.65	135	320	370	150	2.85	2.85	2.83	2.83	1.75	1.7	1.75	1.73	4	6	n		y						
25	49	M		y			36	37	37	37	37	3.05	2.1	1.95	2.96	285	360	380	275	2.56	2.56	2.51	2.51	1.9	1.85	1.85	1.85	5	6	2		y						
26	56	M	y				41	35	33	30	30	3.62	2.3	2.12	3.3	200	340	360	180	3.14	3.12	3.12	3.1	1.43	1.48	1.48	1.48	6	7	1	y								
27	44	F				y	39	42	40	38	38	3.81	2.93	2.14	3.55	150	280	375	140	3.16	3.17	3.16	3.16	1.89	1.89	1.87	1.89	5	6	n			y						
28	38	M	y				40	42	42	41	42	3.7	2.62	1.9	3.41	170	330	380	180	3.55	3.53	3.55	3.58	1.26	1.27	1.2	1.26	5	6	1		y						
29	44	F		y			43	47	48	46	46	3.55	2.72	1.87	3.66	190	350	400	200	2.97	2.95	2.97	2.96	1.18	1.15	1.15	1.15	6	7	n		y						
30	69	M	y				35	30	27	26	24	3.24	2.42	1.6	3.36	205	355	415	200	2.84	2.83	2.81	2.86	1.73	1.75	1.7	1.76	6	7	2	y								
31	47	M	y				34	33	29	27	27	3.8	1.45	0.92	2.45	175	370	460	300	3.85	3.86	3.81	3.87	1.18	1.15	1.12	1.13	7	9	4			y						
32	57	M	y				44	48	46	46	47	3.12	2.51	2.14	2.8	280	324	374	295	3.64	3.6	3.54	3.58	1.4	1.45	1.45	0.45	5	7	n			y						
33	54	F	y				36	30	29	27	27	2.9	2.37	1.64	2.26	280	360	400	310	3.35	3.3	3.34	3.3	1.95	1.94	1.9	1.9	7	8	2	y								
34	71	M	y		y		35	32	29	n	n	2.9	1.71	1.32	2.16	290	390	430	300	3.82	3.81	3.8	3.82	1.02	1.02	1	1	8	9	2	y							y	
35	62	F				y	42	41	39	39	40	2.6	2.2	2.05	2.54	300	340	375	340	3.68	3.68	3.7	3.72	1.24	1.23	1.28	1.24	5	7	1			y						
36	63	M	y				35	39	41	41	41	2.91	2.38	2.07	2.43	285	340	380	290	3.54	3.56	3.56	3.57	1.43	1.45	1.4	1.42	5	7	n		y						
37	49	F				y	37	42	41	40	40	3.5	2.56	1.83	3.2	205	330	380	240	2.6	2.65	2.57	2.62	1.53	1.51	1.51	1.47	6	6	1			y						
38	65	M	y				34	31	28	29	27	3.3	2.18	1.54	3.18	240	375	395	255	2.84	2.87	2.81	2.89	1.92	1.9	1.85	1.88	6	6	2	y								
39	60	F		y			35	38	38	38	38	2.96	2.12	1.48	2.29	300	360	400	330	2.55	2.58	2.54	2.55	1.25	1.28	1.22	1.25	5	6	1			y						
40	44	M			y		40	45	45	45	44	3.75	2.6	2.21	3.65	220	335	370	225	2.83	2.84	2.9	2.85	1.7	1.55	1.5	1.53	6	7	n		y						
41	58	M				y	39	42	41	43	45	3.51	2.35	2.18	3.04	195	345	365	170	3.25	3.2	3.18	3.22	1.48	1.43	1.45	1.44	6	7	1		y						
42	56	M	y				35	30	28	31	29	3.14	2.62	1.57	2.37	280	310	400	330	3.1	3.05	3.05	3.15	1.54	1.5	1.42	1.46	7	8	3	y								
43	48	F	y				40	37	35	36	36	3.8	2.24	1.87	2.65	165	335	380	170	2.24	2.16	2.1	2.19	1.33	1.29	1.29	1.35	6	8	2		y						
44	51	M	y				33	30	31	29	30	3.92	2.83	1.55	3.7	155	285	380	175	3.11	3.05	3.05	3.1	1.44	1.4	1.37	1.39	5	7	2			y						
45	48	M				y	39	45	44	42	44	3.17	2.2	1.84	3	185	370	390	195	1.15	1.05	1.05	1.1	1.8	1.73	1.71	1.63	5	7	n			y						
46	50	F		y			40	41	38	40	40	3.32	2.6	2.17	2.94	250	320	370	270	2.26	2.18	2.15	2.25	1.52	1.5	1.45	1.5	6	7	2		y						
47	70	M	y				32	29	25	26	24	3.3	1.82	1.21	2.16	280	385	430	300	2.42	2.38	2.4	2.42	1.15	1.12	1.05	1.1	8	9	3	y								
48	58	F	y				32	36	36	37	37	2.9	2.72	2.29	2.46	315	335	370	300	2.64	2.56	2.5	2.53	1.29	1.26	1.28	1.28	4	6	4			y						
49	45	M	y				35	42	40	39	50	3.76	2.68	3	2	190	280	405	240	3.18	3.11	3.17	3.19	1.88	1.85	1.7	1.75	5	5	n			y						
50	75	F				y	38	35	35	32	30	2.6	2.45	1.55	2.28	330	345	380	310	3.42	3.37	3.4	3.35	1.67	1.64	1.6	1.65	6	7	2	y								

MASTER CHART (Group B)

sr.no	Age	Sex		ECG				Echocardiogram(EF) in %(months)				Free T3 in pg/ml				Reverse T3 in pg/ml				TSH in mIU/L				Free T4 in ng/ml.				Days in icu	Hosp stay	Readmission	Treatment modality			Case mortality				
			AWMI	IPWMI	LWMI	NSTEMI	At admn	1	4	7	12	Day1	Day4	Day7	Day30	Day1	Day4	Day7	Day30	Day1	Day4	Day7	Dat30	Day1	Day4	Day7	Day30				Medical	PCI	CABG	Admission	1 month	4th	7th	12th
1	46	M		y			50	52	53	52	51	3.85	3.53	3.62	3.7	200	190	195	195	3.42	3.36	3.4	3.45	1.65	1.67	1.64	1.6	4	5			y							
2	52	M	y				48	50	50	50	51	3.55	3.62	3.54	3.5	190	195	190	190	3.15	3.18	3.19	3.13	1.7	1.65	1.62	1.6	4	5			y							
3	58	M				y	57	58	59	59	60	3.45	3.52	3.25	3.28	185	190	190	190	2.6	2.57	2.55	2.58	1.2	1.18	1.15	1.2	4	5		y							
4	35	M		y			50	57	59	59	59	3.25	3.23	3.31	3.21	240	250	235	240	2.48	2.46	2.44	2.45	1.12	1.16	1.16	1.1	5	6	1		y							
5	48	M			y		53	56	55	57	57	3.36	3.36	3.31	3.42	250	255	255	250	1.18	1.15	1.1	1.14	1.9	1.82	1.8	1.85	4	5			y							
6	48	M			y		51	51	50	51	53	3.38	3.29	3.31	3.37	250	255	250	250	2.27	2.23	2.26	2.25	1.34	1.3	1.29	1.3	5	5			y							
7	53	M	y				46	53	54	53	55	3.61	3.45	3.47	3.51	200	210	20	190	3.16	3.14	3.08	3.11	1.55	1.5	1.48	1.45	4	5	2			y						
8	46	M	y				50	54	54	55	54	4.15	3.83	3.85	3.88	140	250	145	140	2.53	2.49	2.49	2.5	1.28	1.22	1.25	1.25	4	5				y						
9	61	M		y			44	48	48	47	47	3.83	3.92	3.9	3.9	160	170	165	165	2.87	2.83	2.82	2.84	1.65	1.63	1.66	1.7	6	7	2		y							
10	63	M	y				50	48	47	45	45	3.11	3.11	3.09	3.1	245	250	245	245	3.26	3.28	3.21	3.25	1.53	1.47	1.46	1.49	6	6		y							
11	54	M			y		64	65	65	65	63	3.93	3.87	3.87	3.91	155	160	155	155	2.81	2.83	2.84	2.89	1.83	1.89	1.84	1.86	4	5		y							
12	62	F				y	47	50	50	50	51	3.82	3.64	3.62	3.74	150	160	155	155	2.64	2.61	2.68	2.65	1.55	1.5	1.5	1.52	5	6			y							
13	35	M	y				49	55	56	56	57	3.46	3.41	3.38	3.35	195	195	195	195	3.75	3.82	3.82	3.79	1.14	1.12	1.12	1.2	4	5				y						
14	55	F				y	53	51	50	52	52	3.11	3.06	3.1	3.12	280	290	280	280	3.38	3.34	3.32	3.36	1.93	1.9	1.86	1.93	5	6			y							
15	59	F		y			46	52	53	52	51	3.47	3.39	3.35	3.02	270	285	270	270	3.52	3.47	3.45	3.56	1.5	1.46	1.48	1.44	5	6				y						
16	62	F				y	55	53	53	52	52	3.41	3.39	3.32	3.37	190	190	190	190	3.8	3.8	3.82	3.8	1.12	1.08	1.05	1.07	4	5	1	y							
17	59	F				y	56	53	53	53	54	3.86	3.73	3.74	3.77	160	185	165	165	2.89	2.85	2.87	2.84	1.7	1.65	1.65	1.65	4	5			y							
18	51	F	y				43	48	48	47	46	3.92	3.85	3.85	3.88	155	175	175	165	2.91	2.95	2.95	2.93	1.19	1.115	1.15	1.13	6	6	1			y						
19	48	M			y		52	57	56	57	57	3.71	3.63	3.65	3.67	190	180	190	190	3.48	3.52	3.5	3.5	1.26	1.22	1.23	1.25	4	5			y							
20	68	F		y			49	49	47	47	47	3.66	3.42	3.45	3.51	205	195	205	205	3.12	3.16	3.12	3.11	1.78	1.75	1.77	1.74	4	6		y							
21	46	F			y		52	50	51	51	51	3.3	3.21	3.25	3.28	230	240	230	230	3.08	3.14	3.11	3.12	1.48	1.44	1.42	1.4	4	6		y							
22	66	M	y				47	52	51	50	50	3.71	3.65	3.65	3.74	150	155	150	150	2.55	2.51	2.52	2.55	1.8	1.73	1.73	1.75	5	5				y						
23	47	F				y	54	53	53	53	53	3.32	3.27	3.25	3.29	230	245	230	230	2.8	2.8	2.76	2.83	1.77	1.72	1.69	1.71	5	6		y							
24	47	M			y		53	57	58	58	58	3.63	3.58	3.55	3.59	190	205	205	205	2.96	2.9	2.85	2.9	1.41	1.4	1.4	1.4	4	6			y							
25	48	F		y			57	55	54	55	55	3.6	3.31	3.25	3.46	185	180	185	185	3.11	3.18	3.22	3.2	1.33	1.3	1.32	1.38	4	6		y							
26	32	M	y				40	45	45	45	46	3.18	3.16	3.11	3.28	175	195	175	175	3.65	3.67	3.68	3.63	1.25	1.21	1.2	1.24	5	7	2			y						
27	48	F				y	51	49	45	44	44	3.22	3.18	3.15	3.19	190	185	190	190	3.21	3.28	3.25	3.22	1.1	1.04	1	1.12	5	6				y						
28	44	M				y	52	50	52	51	51	3	3	2.97	3.15	265	265	265	265	3.3	3.34	3.32	3.35	1.37	1.37	1.34	1.38	4	6			y							
29	35	M			y		55	53	54	52	53	2.83	2.85	2.8	2.92	255	255	255	255	2.25	2.26	2.28	2.27	1.9	1.92	1.88	1.9	5	7		y							
30	78	M		y			45	43	41	40	40	3.37	3.21	3.17	3.25	245	275	250	245	1.2	1.27	1.28	1.25	1.88	1.86	1.85	1.84	5	7	1	y							
31	46	M			y		47	52	52	54	55	3.87	3.75	3.72	3.8	175	180	180	180	2.9	2.83	2.88	2.88	1.41	1.4	1.36	1.38	4	6			y							
32	54	M	y				40	39	38	38	38	2.85	2.82	2.8	2.95	270	280	270	270	3.12	3.15	3.17	3.16	1.2	1.3	1.2	1.1	6	6	2			y						
33	58	M	y				46	50	51	51	51	3.29	3.25	3.27	3.26	250	270	250	250	3.18	3.11	3.09	3.1	1.4	1.35	1.33	1.37	5	7			y							
34	39	F				y	57	55	53	55	55	3.15	3.1	3.07	3.12	240	245	245	240	2.64	2.69	2.65	2.66	1.74	1.7	1.68	1.67	5	7		y							
35	49	F			y		47	49	50	50	50	2.94	2.85	2.87	2.85	280	275	285	280	2.81	2.86	2.84	2.8	1.08	11.02	1.03	1.05	4	6	1		y							
36	58	M		y			42	47	47	49	48	3.18	3.13	3.13	3.1	255	260	255	255	3.72	3.72	3.78	3.74	1.1	1.02	1	1.06	6	7			y							
37	60	M				y	44	47	48	48	48	3.47	3.42	3.41	3.44	250	255	250	250	2.97	2.98	2.96	2.99	1.44	1.42	1.44	1.44	5	6			y							
38	72	M	y		y		39	37	36	35	n	3.1	3.05	3.04	3.08	280	290	300	280	3	3.4	3.3	3.1	1.66	1.62	1.55	1.61	5	6	3	y							y
39	44	F				y	48	50	51	50	50	3.28	3.21	3.21	3.26	240	265	260	250	1.74	1.77	1.79	1.98	1.9	1.83	1.82	1.88	4	5			y							
40	41	F				y	54	53	54	54	54	3.61	3.57	3.51	3.56	210	220	230	215	1.93	1.98	1.98	1.94	1.55	1.48	1.48	1.49	4	5		y							
41	49	M			y		47	48	49	49	49	3.49	3.38	3.39	3.41	200	220	215	210	3.7	3.74	3.72	3.72	1.1	1.08	1.07	1.09	5	6			y							
42	54	M		y			49	50	50	50	50	3.1	3.08	3.09	3.1	255	275	270	270	2.44	2.49	2.45	2.45	1.46	1.43	1.43	1.47	5	6			y							
43	78	M	y				43	41	37	38	n	3.27	3.24	3.21	3.35	265	310	300	280	3.65	3.69	3.6	3.6	1.04	0.98	0.95	1.1	6	7	2	y							
44	50	F			y		43	50	51	51	51	2.96	2.93	2.9	2.94	260	260	255	260	3.15	3.1	3.1	3.11	1.48	1.43	1.42	1.45	5	6			y							
45	48	M				y	44	47	48	48	48	3.41	3.37	3.31	3.36	220	220	245	240	3	3.13	3.11	3.15	1.46	1.4	1.42	1.44	4	5			y							
46	49	F			y		55	55	55	54	54	3.26	3.21	3.18	3.19	265	265	255	260	2.6	2.65	2.63	2.6	1.5	1.45	1.45	1.48	4	4		y							
47	54	M	y				49	53	52	53	53	3.56	3.51	3.45	3.48	225	240	230	225	2.7	2.7	2.65	2.68	1.7	1.65	1.62	1.65	5	6			y							
48	40	M			y		47	54	55	55	55	3.2	3.2	3.11	3.16	245	240	245	240	3.5	3.55	3.53	3.55	1.3	1.3	1.26	1.3	6	6	1		y							
49	68	M				y	49	50	47	47	51	2.94	2.9	2.9	2.93	260	275	260	260	3.11	3.1	3.05	3.1	1.4	1.42	1.4	1.4	5	6	2	y							
50	65	M				y	42	46	45	45	53	3.29	3.21	3.19	3.26	250	265	250	250	3.7	3.75	3.75	3.72	1.25	1.24	1.21	1.23	5	6			y							